ELECTROLYTIC REDUCTION OF *N*-METHYLSUCCINIMIDE AND *N*-ETHYLSUCCINIMIDE.

By **Buhei SAKURAI.**

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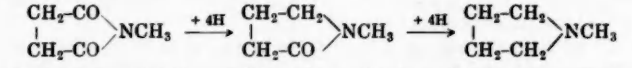
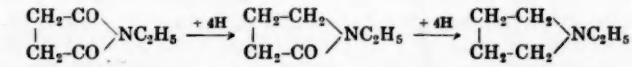
The reduction, especially total reduction, of the cyclic imides of aliphatic acids is very difficult, and it seems to be almost impossible to carry out such reduction through purely chemical methods alone. But it may be accomplished electrolytically by using a lead or a zinc amalgam cathode, which has a strong reducing power. As reported in the preceding paper[1] the present writer carried out electrolytic reduction of succinimide using a zinc amalgam cathode and succeeded in its total reduction with a fairly satisfactory yield of pyrrolidine; and then he proceeded to similar reduction with *N*-methylsuccinimide and *N*-ethylsuccinimide. In these cases reduction goes through the same process as in the case of succinimide:



N-Methylsuccinimide *N*-Methylpyrrolidone *N*-Methylpyrrolidine



N-Ethylsuccinimide *N*-Ethylpyrrolidone *N*-Ethylpyrrolidine

E. Spath[2] and his collaborator reduced several derivatives of succinimide using a very high current density and a lead cathode prepared with special care, and succeeded in total reduction, corresponding reduction products being obtained. A. Luckes[3] reduced *N*-methylsuccinimide in sulphuric acid solution with a current of 0.1 amp./sq. cm., and obtained *N*-methylpyrrolidone.

The present writer tried electrolytic reduction of *N*-methylsuccinimide, using a zinc amalgam cathode[4] in a 50% sulphuric acid solution, at a current density as high as 100–125 amp./100 sq. cm., all the while avoiding any rise of temperature, and thus could carry the reduction over the stage of *N*-methylpyrrolidone and obtain *N*-methylpyrrolidine.

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(1) B. Sakurai, this Bulletin, **10** (1935), 311.
(2) E. Spath and F. Breush, *Monatsh.*, **50** (1928), 349.
(3) R. Luckes, *Collection Czechoslov. Chem. Comm.*, **2** (1930), 531–44.
(4) B. Sakurai, this Bulletin, **7** (1932), 155.

As for *N*-ethylsuccinimide, as far as the present writer knows, no reports on its electrolytic reduction have been published. In the first place a 10% sulphuric acid solution, a lead cathode, and a current of 2.5 amp./100 sq. cm. were used, and the cathodic solution was extracted with chloroform without interfering with its acidity following the example of Lyman[5], the reduction product being thus easily separated. The product was subjected to distillation under reduced pressure. A liquid, which distilled at 107° under 20 mm. was ascertained to be *N*-ethylpyrrolidone by its chemical properties and the results of analysis. Then the concentration of sulphuric acid was increased to 50%, the current density was raised to 100 amp./100 sq. cm., and a zinc amalgam cathode was used to effect a powerful reduction and the experiment resulted in the formation of *N*-ethylpyrrolidine.

Experimental.

The materials for electrolysis were prepared according to the method of Ladenberg[6].

1. **Complete Reduction of *N*-Methylsuccinimide.** Cathode: zinc amalgam placed in a cylindrical vessel of biscuit, area 15 sq. cm.; cathodic solution: 3 g. of methylsuccinimide dissolved in 100 c.c. of 50% sulphuric acid; anode: cylindrical lead; anodic solution: 50% sulphuric acid; current density: 133 amp./100 sq. cm.; temperature: below 30°; time of electrolysis: 8 hours; current quantity: 224 F./mol.

As the rise of temperature has a harmful influence upon electrolysis as in the case of succinimide, a spiral lead tube was inserted in the cylindrical vessel of biscuit which contained the solution, cold water was passed rapidly through the lead spiral, and the apparatus was immersed in water, so that it was cooled from both inside and outside, while the cathodic solution was constantly stirred throughout the electrolysis.

When the electrolysis was over, the cathodic solution was taken out and shaken with a small quantity of chloroform, unchanged substances and *N*-methylpyrrolidone being thus extracted. The solution was then made strongly alkaline by adding a caustic soda solution and then was subjected to steam distillation. *N*-Methylpyrrolidine, the complete reduction product, distilled over with vapour. The distillate was made acid with hydrochloric acid. From the solution the gold salt of *N*-methylpyrrolidine was obtained in a bright yellow substance in the yield of 8 86%. The gold salt melted at 215°. (Found: Au, 46.5. Calc. for $C_6H_{12}N \cdot AuCl_4$: Au, 46.3%.) Its picrate was found to melt at 220°.

2. **Partial Reduction of *N*-Ethylsuccinimide.** Cathode: cylindrical lead plate of 100 sq. cm. placed in a cylindrical vessel of biscuit; cathodic solution: 10 g. of ethylsuccinimide dissolved in 100 c.c. of 10% sulphuric acid solution; anode: lead plate; anodic solution: 10% sulphuric acid solution; current density: 3.0 amp./100 sq. cm.; temperature: 28°; time of electrolysis: 21 hours; current quantity: 29.9 F./mol.

The electrolytic apparatus was placed in water, but this time the cooling from inside was dispensed with. Stirring was again continued during electrolysis.

After the electrolysis was finished, the cathodic solution was treated with chloroform to extract *N*-ethylpyrrolidine. When the chloroform was distilled off, about 8 g. of a liquid remained. When this liquid was subjected to vacuum distillation, 6 g. of a liquid

(5) Lyman, *J. Am. Chem Soc.*, **55** (1933), 295–8.
(6) Ladenberg, *Ann.*, **215** (1882), 211.

distilling at 107° under 20 mm. was obtained. Its specific gravity was 1.0553, and when it was dissolved in 50% sulphuric acid and was oxidized with potassium permanganate solution, it changed back into *N*-ethylsuccinimide. On the other hand, when it was dissolved in 50% sulphuric acid and was electrolytically reduced under the conditions which will be described in the next experiment, it changed into *N*-ethylpyrrolidine. (Found: C, 62.3; H, 10.2; N, 11.98. Calculated for $C_6H_{11}ON$: C, 63.7; H, 9.37; N, 12.39%.) From the above results this substance was evidently *N*-ethylpyrrolidone where only one carbonyl group had undergone reduction.

3. **Complete Reduction of N-Ethylsuccinimide.** The conditions of the electrolysis and the treatment of the product after electrolysis were almost the same as in the case of N-methylsuccinimide. The double gold chloride of *N*-ethylpyrrolidine obtained in the yield of 18.3%. (Found: Au, 44.84. Cal. for $C_6H_{14}NAuCl_4$: Au, 44.87%.) Its picrate, closely resembling that of *N*-methylpyrrolidine, was bright yellow needle crystals and melted at 185°. These and other properties all well agree with those observed by Brown[7].

In conclusion the writer expresses his sincere thanks to Dr. Motooki Matsui, President of the Kyoto Imperial University, for his helpful advice.

ÜBER DIE DAMPFPHASEHYDROLYSE.[1]

Von Shigeaki YAMASAKI.

Eingegangen am 2. November 1935. Ausgegeben am 28. Februar 1936.

In einer früheren Arbeit[2] hat der Verfasser zusammen mit T. Titani gefunden, dass der organische Ester wie Äthylacetat oder Benzylchlorid im Dampfzustand durch den Wasserdampf nicht hydrolysiert wird. Anschliessend daran wurde untersucht, ob dieselbe Reaktion durch den Zusatz von homogenen Katalysatoren[3] oder Gasionen beschleunigt werde. Obwohl der Versuch noch nicht abgeschlossen ist und die bisherigen Ergebnisse sich als negativ erwiesen, erfolgt hier nur eine kurze Mitteilung, weil der Verfasser an der Fortführung der Versuche im hiesigen Laboratorium verhindert ist.

Die verwendeten Katalysatoren waren Chlorwasserstoff und Jod. Der erste wurde als 5 N wässrige Lösung und der letzte als Esterlösung dem dampfförmigen Gemisch aus Äthylacetat und Wasser zugesetzt und bei 200°C. während verschiedener Zeitdauer erhitzt. Die sonstige Versuchsanordnung sowie die analytische Methode des Reaktionsprodukts waren genau dieselben

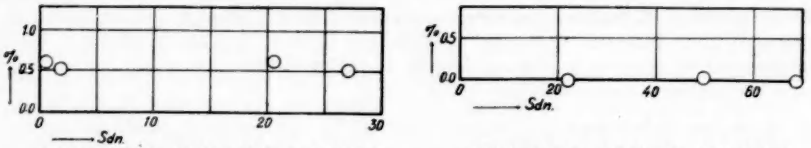
(7) J. W. Brown, *Ber.*, **44** (1911), 1252–60.

(1) Ergänzung der Arbeit von S. Yamasaki und T. Titani, dieses Bulletin, **9** (1934), 501.

(2) *Loc. cit.*

(3) Die heterogene Katalyse für die Hydrolyse sowie Esterbildung in Dampfphase ist schon wohl bekannt.

wie früher. Die Versuchsresultate ergaben sich ebenfalls als negativ, wie aus Abb. 1 ersichtlich ist, wo die zersetzten Mengen des Esters im Vergleich zur Versuchsdauer eingetragen sind.



$CH_3COOC_2H_5+H_2O+HCl$, bei 200°C. $CH_3COOC_2H_5+H_2O+J_2$, bei 200°C.

Abb. 1.

Im zweiten Versuch wurde versucht die Reaktionen durch den Zusatz von Gasionen zu katalysieren. Zu diesem Zweck wurde das Reaktionsgemisch bei 200°C. durch Röntgenstrahlen aus Molybden-Antikathode bestrahlt. Die Versuchsergebnisse sind in Tabelle 1 zusammengestellt.

Tabelle 1. Versuche mit Röntgenstrahlen.

Reaktionsgemisch	Intensität der Röntgenstrahlen		Versuchsdauer in Stunden	Prozentuale Zersetzung (%)
	Kilovolt	Milliamp.		
$CH_3COOC_2H_5$ allein	20	1	1	0.00
$CH_3COOC_2H_5+H_2O$	20	1	1	0.00
$CH_3COOC_2H_5+H_2O+HCl$	20	1	1	0.50
wie oben	20	1	1.6	0.45
$CH_3COOC_2H_5+H_2O+J_2$	20	1	1	0.03
wie oben	20	1	1	0.04
$C_2H_5Br+H_2O$	20	1	1	0.05
wie oben	30	4	2	0.03
$C_6H_5Br+H_2O$	20	1	1	0.06

Die Halogen-haltigen Verbindungen wurden zugesetzt oder verwendet um das Absorptionsvermögen des Reaktionsgemisches für die Röntgenstrahlen zu erhöhen. Die Versuchsdauer war sehr kurz im Vergleich mit den der erst genannten Versuche, aber mindestens wurden während dieser Zeitdauer keine Spuren einer hydrolytischen Reaktion innerhalb des Messfehlers gefunden.

Herrn Prof. T. Titani habe ich für die Anregung zu dieser Arbeit herzlichst zu danken. Ebenso bin ich Herrn Prof. I. Nitta, der die Röntgenapparat zur Verfügung gestellt hat, zum besten Dank verpflichtet.

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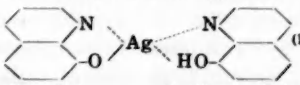
DI-8-OXYCHINOLIN-INNERKOMPLEXSALZ DES ZWEIWERTIGEN SILBERS[1].

Von Yuichi NAKATSUKA.

Eingegangen am 4. November 1935. Ausgegeben am 28. Februar 1936.

Wir kennen bisher noch recht wenige Salze von zweiwertigem Silber. Man findet in der Literatur etwa folgende: Tetrapyridinsilber(II)-persulfat[2] und -nitrat[3]; Di-*o*-phenanthrolin-silber (II)-persulfat, -chlorat, -perchlorat, -nitrat und -hydrosulfat[4]; Di-α,α'-dipyridylsilber (II)-persulfat, -hydrosulfat, -perchlorat und -nitrat[5]; Tri-α,α'-dipyridylsilber(II)-nitrat, -chlorat und -perchlorat[6]; Penta-α,α'dipyridyldisilber (II)-persulfat[6]; Picolinsaures Silber(II)[7]; Chinolinsaures Silber(II)[8]; Silber(II)-fluorid[9]. Ausgenommen von Silber(II)-fluorid, das direkt aus den Bestandteilen dargestellt wurde, wurden alle anderen Salze durch anodische Oxydation bzw. durch Oxydation mittels Persulfates gewonnen.

Mir gelang es nun, das Di-8-oxychinolinsilber(II) auf ganz anderem Wege, d.h. ohne Gebrauch von besonderem Oxydationsmittel darzustellen, worüber in der vorliegenden Arbeit ebenso wie über die entsprechenden Silber(I)- und Kupfer(II)-verbindungen berichtet wird.

Fügt man zu einer abgekühlten Silberacetatlösung eine alkoholische Lösung von 8-Oxychinolin, so erhält man gelbes Di-8-oxychinolinsilber(I) von der Formel  [10]. Falls die Silberacetatlösung dagegen heiss ist, so scheiden sich grüne Kristalle

(1) Vorgetragen am 5. April 1935 auf der Hauptversammlung der Japanischen Chemischen Gesellschaft.

(2) G. A. Barbieri, *Gazz. chim. ital.* **42** II (1912), 7.

(3) G. A. Barbieri, *Ber.*, **60** (1927), 2424.

(4) W. Hieber u. F. Mühlbauer, *Ber.*, **61** (1928), 2149.

(5) G. T. Morgan u. F. H. Burstall, *J. Chem. Soc.*, **1930**, 2594; G. A. Barbieri, *Atti accad. Lincei*, [6], **16** (1932), 44.

(6) G. T. Morgan u. F. H. Burstall, a.a.O.

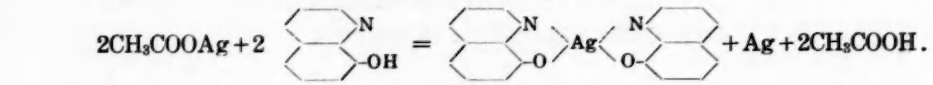
(7) G. A. Barbieri, *Atti accad. Lincei*, [6], **17** (1933), 1078.

(8) A. Burada, *Ann. Sci. Univ. Jassy*, **20** (1934), 71.

(9) O. Ruff u. M. Giese, *Z. anorg. allgem. Chem.*, **219** (1934), 143.

(10) Der räumliche Bau dieses Salzes wurde neulich als tetraedrisch festgestellt: Fr. Hein u. H. Regler, *Naturwiss.*, **23** (1935), 320.

von Di-8-oxychinolinat des zweiwertigen Silbers zusammen mit metallischem Silber nach folgender Gleichung ab:



Wie die Gleichung zeigt, oxydiert das eine von zwei einwertigen Silberatomen das andere zum zweiwertigen Zustand, und anderseits scheidet sich dieses selbst in metallischem Silber aus. Behandelt man das Komplexsalz-Silber-Gemisch mit Pyridin und lässt die pyridinische Lösung eindunsten, so kristallisiert das Salz mit einem Mol Pyridin rein aus.

8-Oxychinolin lässt sich, wie allgemein bekannt, sehr leicht bromometrisch titrieren[11], wobei ein Mol desselben vier Atomen Brom entspricht. Dementsprechend verbraucht ein Mol Di-8-oxychinolinsilber (I) acht Atome Brom in einer Säurelösung, damit es völlig bromiert wird[12]. In gleicher Weise bei Anwesenheit von Bromwasserstoffsäure behandelt, oxydiert Di-8-oxychinolinsilber (II) dagegen Bromwasserstoff, indem ein Atom Brom pro Mol Salz frei wird. Daher verbraucht in diesem Falle ein Mol des Salzes ein Atom Brom weniger als die entsprechende Silber (I)-verbindung, wie folgende Gleichungen zeigen:

$$Ag^{I}(C_9H_6NO)(C_9H_7NO) + 8Br = 2C_9H_5NOBr_2 + AgBr + 3HBr,$$

$$Ag^{II}(C_9H_6NO)_2 + 7Br = 2C_9H_5NOBr_2 + AgBr + 2HBr.$$

Aus diesem Grunde kann man also sehr leicht beweisen, dass das Silber im zweiwertigen Zustand existiert.

Di-8-oxychinolinkupfer (II) kristallisiert aus Pyridin auch mit einem Mol Pyridin. Di-8-oxychinolinat des einwertigen Silbers bildet ebenfalls ein 1 Mol Pyridin enthaltendes Solvat. Diese drei pyridinhaltigen Salze haben überdies dieselbe säulenförmige Kristallgestalt.

Experimenteller Teil.

Di-8-oxychinolinsilber (I). Man löst 0.6 g. Silberacetat in 150 c.c. heissem Wasser. Nach Zusatz von etwas Natriumacetat fügt man in der Eiskälte unter Umrühren 20 c.c. Alkohol hinzu, der 1 g. 8-Oxychinolin gelöst enthält. Gelbe feine Säulen kristallisieren aus, die abgesaugt, mit Wasser nachgewaschen und auf Ton an der Luft getrocknet werden. Ausbeute fast quantitativ. Löslich in Pyridin und Chloroform, weniger in Alkohol, unlöslich in Wasser. (Gefunden: Ag, 27.31; N, 7.04. Berechnet für $Ag(C_9H_6NO)(C_9H_7NO)$: Ag, 27.17; N, 7.06%.)

(11) R. Berg, *Pharm. Ztg.*, **71** (1926), 1542.
(12) Vgl. R. Berg, *J. prakt. Chem.*, **115** (1927), 1780.

Nach dem Eintragen des Salzes in eine salzsaure Bromkaliumlösung, titriert man es mit Kaliumbromatlösung nach der bromometrischen Methode von Berg[12]. Als Indikator wird aber eine alkoholische Methylrotlösung nach Kolthoff verwendet. 0.0864 g. Subst. verbrauchten 17.48 c.c. N/10. Brom (Ber. 17.41 c.c.).

Trägt man das Salz in wenig Pyridin ein, so löst es sich zunächst, aber bald danach fällt das Salz mit einem Mol Pyridin in gelben Säulen aus. (Gefunden: Ag, 22.80; N, 8.88. Berechnet für $[Ag(C_9H_6NO)(C_9H_7NO)]\cdot C_5H_5N$: Ag, 22.66; N, 8.83%.)

Di-8-oxychinolinsilber (II). Die Darstellungsvorschrift ist wie beim Silber(I)-salze. Man löst jedoch etwas mehr als 1.2 g. Silberacetat in 200 c.c. heissem Wasser, und beim Zusatz von alkoholischem 8-Oxychinolin wird die Acetatlösung etwa auf 60° gehalten. Zuerst fällt Di-8-oxychinolinat des einwertigen Silbers aus, dessen Silber aber sogleich zum zweiwertigen Zustand oxydiert wird. Das dabei entstandene metallische Silber scheidet sich teilweise mit dem Salze gemischt und teilweise auch als Silberspiegel an der Gefässwand aus. Das Salz bildet grasgrüne viereckige Tafeln.

Zur Ermittlung der Zusammensetzung des Komplexsalzes und der Zweiwertigkeit des Silbers desselben wurde mit einem gut zerriebenen und möglichst einheitlich zusammengerührten Komplexsalz-Silber-Gemisch zuerst die Stickstoffbestimmung durchgeführt. (Gefunden: N, 5.75%.) Wenn das Komplexsalz kein Kristallwasser hat, so sollte das Gemisch von der Zusammensetzung Silber 18.72% + Komplexsalz 81.28% denselben Stickstoff- und 40.86%igen Silbergehalt ergeben. Analysenergebnisse mit derselben Probe waren folgende: Ag, 40.90%; 0.0677 g. Gemisch verbrauchten 9.80 c.c. N/10 Brom. Berechnet aus dem Stickstoffgehalt für das genommene Gemisch: 9.73 c.c. Die Analysen stimmen also mit den berechneten Werten gut überein, und daraus kann man mit Sicherheit schliessen, dass das Komplexsalz kristallwasserfrei ist und das Silber in zweiwertiger Form vorliegt.

Das Salz löst sich nicht in Wasser, ist aber löslich in Pyridin und in Chloroform. Um das Salz vom beigemengten metallischen Silber zu trennen, schüttelt man das Gemisch gut mit Pyridin. Nach dem Abfiltrieren des metallischen Silbers lässt man die pyridinische Lösung im Vakuum eindunsten, wobei das Komplexsalz in grasgrünen Säulen auskristallisiert. (Gefunden: Ag, 22.98, 22.66; N, 8.85. Berechnet für $[Ag(C_9H_6NO)_2]\cdot C_5H_5N$: Ag, 22.71; N, 8.85%.) Bromometrie wurde wie beim entsprechenden Silber(I)-salz durchgeführt. 0.0994 g. Subst. verbrauchten 14.60 c.c. N/10 Brom. (Berechnet: 14.64 c.c.).

Di-8-oxychinolinkupfer (II)[13]. Fällt man eine natriumacetathaltige Kupferacetatlösung mit einer alkoholischen Lösung von 8-Oxychinolin, so scheidet sich Di-8-oxychinolinkupfer in einem blassgrünen Kristallpulver ab. Das Salz hat zwei Mol Kristallwasser (Salz I). (Gefunden: Cu, 16.77, 16.25; N, 7.26; H_2O, 9.40. Berechnet für $[Cu(C_9H_6NO)_2]\cdot 2H_2O$: Cu, 16.40; N, 7.23; H_2O, 9.29%.) 0.1015 g. Subst. verbrauchten 18.16 c.c. N/10 Brom. (Berechnet: 18.32 c.c.) Fällt man dagegen in der Siedehitze, so erhält man gelbgrüne Nadeln. Dieses Salz enthält ein halbes Mol Wasser (Salz II). (Gefunden: Cu, 17.50; H_2O, 2.0, 3.0. Berechnet für $[Cu(C_9H_6NO)_2]\cdot \frac{1}{2}H_2O$: Cu, 17.63; H_2O, 2.50%.)

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(13) Bisher wurde nur das Salz als kristallwasserfrei beschrieben: Zd. H. Skraup, *Monatsh.*, **3** (1882), 541; G. Bargellini u. I. Bellucci, *Gazz. chim. ital.*, **53** (1923), 605.

Trägt man eines der beiden Salze I und II in wenig Pyridin ein, so fällt das Salz kristallwasserfrei als braungrüne seckseitige Tafeln (Salz III). (Gefunden: Cu, 17.86; N, 8.02. Berechnet für $Cu(C_9H_6NO)_2$: Cu, 18.08; N, 7.97%.) Wenn man dagegen viel Pyridin verwendet, so löst sich das zuerst ausgeschiedene Salz wieder. Aus dieser Lösung erhält man beim Eindunsten grasgrüne Säulen, die ein Mol Pyridin pro Mol Salz enthalten (Salz IV). Dieses Salz verliert ziemlich schnell seinen Pyridingehalt. (Gefunden: Cu, 14.91; N, 9.71; Pyridin, 19.72. Berechnet für $[Cu(C_9H_6NO)_2]\cdot C_5H_5N$: Cu, 14.76; N, 9.76; Pyridin, 18.35%.)

Herrn S. Murayama spreche ich hier meinen herzlichen Dank für seine Hilfe aus.

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ÜBER DIDIMETHYLGLYOXIM-DIAMMIN-KOBALT (III)-SALZE UND IHRE KONFIGURATION.[1]

Von Yuichi NAKATSUKA und Hirosi IINUMA.

Eingegagen am 5. November 1935. Ausgegeben am 28. Februar 1936.

Feigl und Rubinstein[2] erhielten grüne Kristalle von der Formel $[Co(DH_2)_2Cl_2]$[3] aus einer alkoholischen oder acetonischen Lösung von Kobaltchlorid und Dimethylglyoxim. Wenn man aber eine völlig wasserfreie acetonische Lösung von frisch entwässertem Kobaltchlorid und Dimethylglyoxim eindunsten lässt, so kristallisiert dagegen nach Thilo und Heilborn[4] ein rotes mit dem Feiglschen grünen Salz isomeres echtes Chlorid $[Co(DH_2)_2]Cl_2$ aus. Thilo und Heilborn[4] haben überdies festgestellt, dass im Feiglschen Salz zwei Chloratome trans-Stellungen besetzen, also zwei Dimethylglyoxime plan konfiguriert sein müssen.

Ausgehend von diesen beiden Salzen, haben wir in der vorliegenden Arbeit (1) einige neue Kobalt(III)-komplexsalze von der allgemeinen Formel $[CoA_2(DH)_2]X$[5] dargestellt, und (2) die Konfiguration der

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(1) Gekürzte Übersetzung der schon in Japanisch veröffentlichten Arbeit, *J. Chem. Soc. Japan*, **55** (1934), 630.

(2) *Ann.*, **433** (1923), 183. Vgl. dazu Hieber u. Leutert, *Ber.*, **60** (1927), 2296; Thilo u. Heilborn, *Ber.*, **64** (1931), 1441.

(3) DH_2 = Dimethylglyoxim, DH = einwertiger Dimethylglyoximrest.

(4) a.a.O.

(5) A = NH_3 bzw. einwertiges Amin; X = einwertiger Säurerest.

schon beschriebenen und auch der von uns zum ersten Mal erhaltenen Salze dieser Reihe daraufhin bewiesen, dass zwei Dimethylglyoximreste immer sehr fest plan koordiniert sind, wie dies bei den zwei Dimethylglyoximen im Feiglschen Salz des zweiwertigen Kobalts der Fall ist.

Frühere Untersuchungen über die Salze der Reihe wurden fast alle von Tschugaeff[6] durchgeführt. Er erhielt $[Co(NH_3)_2(DH)_2]Cl$ aus $[Co(NH_3)_6]Cl_3$ und Dimethylglyoxim. Die anderen Salze wurden im wesentlichen direkt aus den Bestandteilen dargestellt, also z.B. $[Copy_2(DH)_2]Cl$ durch Oxydation mittels Luftsauerstoffes einer Mischung alkoholhaltiger Lösungen von Kobaltchlorid, Dimethylglyoxim und Pyridin.

Beato und Brugger[7] erhielten 1929 Komplexsalze der Reihe (A = Anilin bzw. *o*- und *p*-Toluidin) direkt aus der alkoholischen Lösung der Bestandteile, aber sie benutzten die Salze als Nachweisreagenzien von Polysulfid und bestimmten die Zusammensetzung selbst nicht.

Wir haben uns der oben erwähnten Methode von Beato und Brugger bedient, d.h. eine gemischte alkoholische Lösung von Kobaltchlorid und Dimethylglyoxim wurde nach Zusatz von Amin mit Luft oxydiert. Auf diese Weise haben wir zuerst das Chlorid, dann durch doppelte Umsetzung das Bromid, Jodid, Rhodanid, Nitrat, saure Sulfat und neutrale Sulfat dargestellt. Als Amine wurden Ammoniak, Anilin, *o*- und *p*-Toluidin, *m*-Xylidin, und α- und β-Naphthylamin gebraucht. Das von uns so erhaltene Salz $[Co(NH_3)_2(DH)_2]Cl$ war dasselbe wie das von Tschugaeff aus $[Co(NH_3)_6]Cl_3$ gewonnene.

Wie im experimentellen Teil beschrieben wird, koordinieren alle diese Amine ausserordentlich leicht am Zentralkobaltatom. Wenn nun ein Molekül *o*-Phenylendiamin als zweizähliger Ligand anstelle von zwei A treten würde, müsste es sich natürlich in cis-Stellung binden, vorausgesetzt dass zwei Dimethylglyoximreste nicht plan konfiguriert sind. Ein solches Salz konnte aber nie erhalten werden, sondern immer trat *o*-Phenylendiamin als einzähliger Ligand an das Kobaltatom wie in dem Salz $[Coph_2(DH)_2]Cl$[8]. Daraus folgt, dass die zwei Dimethylglyoximreste in einer Ebene liegen und infolgedessen zwei A in den Salzen $[CoA_2(DH)_2]X$ trans-Stellungen besetzen müssen.

Wir haben noch ein Salz von der Zusammensetzung $Co(DH)_2Cl,ph$ erhalten. Dieses Salz enthält aber kein ionogenes Chlor, was sich durch

(6) *Z. anorg. Chem.*, **46** (1905), 144; *Ber.*, **39** (1906), 2692. Vgl. dazu noch „Gmelins Handbuch der anorganischen Chemie", 58.B, S.276f.

(7) *Anales Soc. Espanola Fisica Quim.*, **27** (1929), 822.

(8) ph = *o*-Phenylendiamin.

Schäumen beim Eintragen in konzentrierte Schwefelsäure erkennen lassen würde. Aus diesem Grunde hat das Salz die Formel $[Coph(DH)_2Cl]$ und nicht $[Coph(DH)_2]Cl$. Auch hier reagiert *o*-Phenylendiamin als einzähliger Ligand.

Auch wenn man von dem Thiloschen roten Salz $[Co(DH_2)_2]Cl_2$ ausgeht, kann man keine anderen Salze der allgemeinen Formel $[CoA_2(DH)_2]Cl$ erhalten. Wenn man also z.B. nach Einleitung von trockenem Ammoniak in eine acetonische Lösung von $[Co(DH_2)_2]Cl_2$ mit getrockneter Luft oxydiert, oder anstatt des Ammoniaks Anilin gebraucht, erhält man immer dieselben Salze wie oben.

Falls man *o*-Phenylendiamin als Amin verwendet, scheiden sich zuerst gelbe Nadeln aus. Diese Kristalle verschwinden allmählich mit dem Luftzutritt, und es gelingt nicht, aus der Lösung ein kristallinisches Komplexsalz zu erhalten. Diese gelben Nadeln haben die Formel $[Coph(DH_2)_2(OH_2)]Cl_2, CH_3{\cdot}CO{\cdot}CH_3$, worin Kobalt also zweiwertig ist. Denn dasselbe Salz wird ebenso erhalten, wenn man in einer Stickstoffatmosphäre arbeitet. Auch ist das Salz durch Säuren sehr leicht zersetzbar, während Kobalt(III)-dimethylglyoxim-komplexsalze im allgemeinen beständig gegen Säuren sind. Das Salz verliert kein Gewicht im Vakuum über konzentrierter Schwefelsäure oder bei 110° und reagiert deutlich sauer in wässriger Lösung. Diese Reaktion kann folgendermassen gedeutet werden:

$$[Coph(DH_2)_2(OH_2)]Cl_2 \rightarrow [Coph(DH_2)_2(OH)]Cl + HCl.$$

Aus dem oben beschriebenen kann man schliessen, dass in allen bisher erhaltenen und von uns neu dargestellten Kobalt(III)-komplexsalzen von der allgemeinen Formel $[CoA_2(DH)_2]X$ zwei Dimethylglyoximreste sehr fest plan konfigurieren, und daher zwei A trans-Stellungen besetzen.

Experimenteller Teil.

Allgemeine Darstellungsmethoden der Salze $[CoA_2(DH)_2]X$. Zur Darstellung des Chlorids löst man 1 g. kristallisiertes Kobaltchlorid in 15 c.c. warmem Alkohol, der 1 g. Dimethylglyoxim gelöst enthält. Nach dem Erkalten trägt man etwa 4 Mole Amin auf 1 Mol Kobaltchlorid ein und oxydiert das Gemisch 5 Minuten lang durch einen starken Luftstrom oder lässt 30 Minuten unter häufigem Umrühren an der Luft stehen. Das Chlorid, das sich sehr leicht ausscheidet, wird nach dem Abfiltrieren aus warmem Wasser umkristallisiert. Fügt man dabei etwas Natriumchlorid hinzu, so wird das Salz mit besserer Ausbeute erhalten.

Das Bromid, Jodid, Rhodanid bzw. Nitrat kristallisiert mit guter Ausbeute aus einer warmen konzentrierten Lösung des Chlorids beim Zusatz eines Überschusses an Kaliumbromid, Kaliumjodid, Kaliumrhodanid bzw. Natriumnitrat.

Auf diese Weise kann man jedoch das Sulfat wegen seiner grossen Löslichkeit nicht rein erhalten. Wenn man eine alkoholische oder acetonische Lösung von Dimethylglyoxim und Amin, in welcher gepulvertes kristallisiertes Kobaltsulfat suspendiert ist, mit Luft oxydiert, erhält man unreines Sulfat. Um daraus das Sulfat rein darzustellen, ist es empfehlenswert, über das saure Sulfat zu gehen. Wenn man also zu einer konzentrierten Lösung des unreinen Sulfates halbkonzentrierte Schwefelsäure im Überschuss fügt, so kristallisiert reines saures Sulfat in guter Ausbeute aus. Dasselbe saure Sulfat erhält man auch, wenn man eine konzentrierte warme Lösung des Chlorids oder das in wenig Wasser suspendierte Chlorid mit Schwefelsäure reagieren lässt. Fügt man zu dem in möglichst wenig Wasser eingetragenen sauren Sulfat die berechnete Menge oder einen geringen Überschuss an Natriumkarbonatlösung und lässt das Gemisch erkalten oder versetzt es mit etwas Natriumsulfat, so scheidet sich das neutrale Sulfat rein aus.

Didimethylglyoxim-diammin-kobalt (III)-salze. *Chlorid.* Die Darstellungsmethode ist die gleiche wie die oben angegebene allgemeine Vorschrift, wobei Ammoniak als konzentrierte Lösung gebraucht wird. Dabei scheiden sich gelbe Nadeln aus. Aus Wasser umkristallisiert, erhält man sie rein als viereckige Tafeln. Gut löslich in Wasser, in Alkohol etwas löslich. (Gef.: Co, 13.12; H_2O, 20.07. Ber. für $[Co(NH_3)_2(DH)_2]Cl,5H_2O$: Co, 13.15; H_2O, 20.04%.)

Bromid. Gelbe Tafeln, schlecht löslich in Wasser und Alkohol. (Gef.: Co, 14.60. Ber. für $[Co(NH_3)_2(DH)_2]Br$: Co, 14.64%.)

Jodid. Gelbe Nadeln, schwer löslich in Wasser, Alkohol und Aceton. (Gef.: Co, 13.15. Ber. für $[Co(NH_3)_2(DH)_2]I$: Co, 13.12%.)

Rhodanid. Gelbe Schuppen, schwer löslich wie das Jodid. (Gef.: Co, 14.81; H_2O, 4.52. Ber. für $[Co(NH_3)_2(DH)_2]SCN,H_2O$: Co, 14.80; H_2O, 4.66%.)

Nitrat. Gelbe Nadeln, ziemlich gut löslich in Wasser, schwer in Alkohol. (Gef.: Co, 15.36. Ber. für $[Co(NH_3)_2(DH)_2]NO_3$: Co, 15.33%.)

Didimethylglyoxim-dianilin-kobalt (III)-salze. *Chlorid.* Zuerst als Nadeln erhältlich; aus Wasser umkristallisiert gelbbraune Prismen, ziemlich gut löslich in Wasser, Alkohol, und Aceton. (Gef.: Co, 10.18; H_2O, 12.32. Ber. für $[Co(C_6H_7N)_2(DH)_2]Cl,4H_2O$: Co, 10.12; H_2O, 12.35%.)

Bromid. Orangefarbene Nadeln, nicht gut löslich in Wasser und Alkohol. (Gef.: Co, 10.70; N, 15.32. Ber. für $[Co(C_6H_7N)_2(DH)_2Br$: Co, 10.63; N, 15.13%.)

Jodid. Braune Nadeln, wenig löslich in Wasser und Alkohol. (Gef.: Co, 9.76; N, 14.25. Ber. für $[Co(C_6H_7N)_2(DH)_2]I$: Co, 9.81; N, 13.95%.)

Rhodanid. Orangefarbene Tafeln, schwer löslich in Wasser. (Gef.: Co, 10.45; N, 17.79; H_2O, 3.17. Ber. für $[Co(C_6H_7N)_2(DH)_2]SCN,H_2O$: Co, 10.70; N, 17.78; H_2O, 3.27%.)

Nitrat. Orangefarbene Nadeln, nicht gut löslich in Wasser und Alkohol. (Gef.: Co, 11.08; H_2O, 6.76. Ber. für $[Co(C_6H_7N)_2(DH)_2]NO_3,2H_2O$: Co, 10.97; H_2O, 6.29%.)

Saures Sulfat. Graubraune Tafeln, ziemlich gut löslich in Wasser, wenig in Alkohol und Aceton. (Gef.: Co, 9.69; SO_4, 15.98; N, 13.83; H_2O, 5.28. Ber. für $[Co(C_6H_7N)_2(DH)_2]_2SO_4,H_2SO_4,3\frac{1}{2}H_2O$: Co, 9.79; SO_4, 15.88; N, 13.90; H_2O, 5.30%.)

Neutrales Sulfat. Gelbe Säulen, sehr gut löslich in Wasser, auch gut in Alkohol. (Gef.: Co, 10.09; N, 14.60; H_2O, 10.85. Ber. für $[Co(C_6H_7N)_2(DH)_2]_2SO_4,7H_2O$: Co, 10.05; N, 14.34; H_2O, 10.73%.)

Didimethylglyoxim-di-*o*-toluidin-kobalt(III)-salze. *Chlorid.* Sechseckige Prismen, ziemlich gut löslich in Wasser und Alkohol. (Gef.: Co, 9.69; H_2O, 12.10. Ber. für $[Co(C_7H_9N)_2(DH)_2]Cl,4H_2O$: Co, 9.67; H_2O, 11.80%.)

Bromid. Gelbbraune Säulen, wenig löslich in Wasser. (Gef.: Co, 9.76; H_2O, 3.02. Ber. für $[Co(C_7H_9N)_2(DH)_2]Br, H_2O$: Co, 9.82; H_2O, 2.99%.)

Jodid. Orangefarbene Nadeln, schwer löslich in Wasser. (Gef.: Co, 9.36; N, 13.00. Ber. für $[Co(C_7H_9N)_2(DH)_2]I$: Co, 9.38; N, 13.32%.)

Rhodanid. Orangefarbene Nadeln, schwer löslich in Wasser. (Gef.: Co, 10.37; N, 16.87; H_2O, 3.40. Ber. für $[Co(C_7H_9N)_2(DH)_2]SCN,H_2O$: Co, 10.19; N, 16.90; H_2O, 3.11%.)

Nitrat. Braune Säulen, nicht gut löslich in Wasser und Alkohol. (Gef.: Co, 10.52; N, 17.30. Ber. für $[Co(C_7H_9N)_2(DH)_2]NO_3$: Co, 10.44; N, 17.35%.)

Saures Sulfat. Braune Prismen, gut löslich in Wasser. (Gef.: Co, 9.40; SO_4, 15.97; N, 13.77; H_2O, 3.04. Ber. für $[Co(C_7H_9N)_2(DH)_2]_2SO_4,H_2SO_4,2H_2O$: Co, 9.56; SO_4, 15.35; N, 13.61; H_2O, 2.92%.)

Neutrales Sulfat. Gelbe Nadeln, sehr gut löslich in Wasser. (Gef.: Co, 9.02; N, 12.87; H_2O, 16.59. Ber. für $[Co(C_7H_9N)_2(DH)_2]_2SO_4,12H_2O$: Co, 8.96; N, 12.73; H_2O, 16.37%.)

Didimethylglyoxim-di-*p*-toluidin-kobalt(III)-salze. *Chlorid.* Braune Säulen, ziemlich gut löslich in Wasser, wenig in Alkohol und Aceton. (Gef.: Co, 10.68; H_2O, 3.17. Ber. für $[Co(C_7H_9N)_2(DH)_2]Cl,H_2O$: Co, 10.59; H_2O, 3.24%.)

Bromid. Gelbbraune Nadeln. (Gef.: Co, 10.22. Ber. für $[Co(C_7H_9N)_2(DH)_2]Br$: Co, 10.12%.)

Jodid. Gelbbraune Nadeln. (Gef.: Co, 9.46; N, 13.53. Ber. für $[Co(C_7H_9N)_2(DH)_2]I$: Co, 9.37; N, 13.47%.)

Rhodanid. Gelbbraune Nadeln. (Gef.: Co, 10.63; N, 17.41. Ber. für $[Co(C_7H_9N)_2(DH)_2]SCN$: Co, 10.51; N, 17.45%.)

Nitrat. Braune rautenförmige Tafeln, ziemlich gut löslich in Wasser. (Gef.: Co, 10.37. Ber. für $[Co(C_7H_9N)_2(DH)_2]NO_3$: Co, 10.44%.)

Saures Sulfat. Rotbraune sechseckige Prismen, gut löslich in Wasser. (Gef.: Co, 8.74; SO_4, 17.91; N, 12.01; H_2O, 9.37. Ber. für $[Co(C_7H_9N)_2(DH)_2]_2SO_4$, $1\frac{1}{2}H_2SO_4,7H_2O$: Co, 8.59; SO_4, 17.46; N, 12.22; H_2O, 9.11%.)

Neutrales Sulfat. Rotbraune Säulen, sehr gut löslich in Wasser. (Gef.: Co, 9.18; H_2O, 14.35. Ber. für $[Co(C_7H_9N)_2(DH)_2]_2SO_4,10H_2O$: Co, 9.20; H_2O, 14.04%.)

Freie Base. Aus der Lösung des Chlorids oder Sulfats der Reihe mit überschüssigem Alkali als gelbbraune flache Säulen erhältlich, schwer löslich in Wasser, wenig in Aceton, gut in Alkohol. (Gef.: Co, 10.70; H_2O, 6.80. Ber. für $[Co(C_7H_9N)_2(DH)_2]OH,2H_2O$: Co, 10.61; H_2O, 6.48%.)

Didimethylglyoxim-di-*m*-xylidin-kobalt (III)-salze. *Chlorid.* Braune Säulen, ziemlich gut löslich in Wasser, Alkohol, und Aceton. (Gef.: Co, 9.70; H_2O, 6.25. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]Cl,2H_2O$: Co, 9.80; H_2O, 5.98%.)

Bromid. Gelbbraune Nadeln. (Gef.: Co, 9.59; N, 13.56. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]Br$: Co, 9.66; N, 13.74%.)

Jodid. Gelbbraune Säulen. (Gef.: Co, 8.80; H_2O, 2.66. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]I,H_2O$: Co, 8.73; H_2O, 2.66%.)

Rhodanid. Gelbbraune Nadeln. (Gef.: Co, 9.84; N, 16.74. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]SCN$: Co, 10.00; N, 16.63%.)

Nitrat. Braune Prismen. (Gef.: Co, 9.85; H_2O, 3.53. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]NO_3,H_2O$: Co, 9.66; H_2O, 2.95%.)

Sulfat. Entgegen der allgemeinen Vorschrift kann man dieses Salz direkt aus dem unreinen Sulfat durch Umkristallisieren aus Alkohol und Wasser darstellen. Gelbe Tafeln, sehr gut löslich in Wasser. (Gef.: Co, 9.12; N, 12.98; H_2O, 10.55. Ber. für $[Co(C_8H_{11}N)_2(DH)_2]_2SO_4,7\frac{1}{2}H_2O$: Co, 9.13; N, 12.97; H_2O, 10.43%.)

Didimethylglyoxim-di-α-naphthylamin-kobalt(III)-salze. *Chlorid.* Rotbraune Nadeln, ziemlich gut löslich in warmem Wasser. (Gef.: Co, 9.07; H_2O, 5.88. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]Cl,2H_2O$: Co, 9.13; H_2O, 5.60%.)

Bromid. Rotbraune Nädelchen. (Gef.: Co, 8.48; H_2O, 6.00. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]Br,2H_2O$: Co, 8.53; H_2O, 5.21%.)

Jodid. Rotbraunes Pulver. (Gef.: Co, 8.22; H_2O, 1.63. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]I,\frac{1}{2}H_2O$: Co, 8.30; H_2O, 1.27%.)

Rhodanid. Orangefarbenes Pulver, schwer löslich in Wasser. (Gef.: Co, 9.41; N, 15.57. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]SCN$: Co, 9.32; N, 15.49%.)

Nitrat. Rotbraune Säulen, wenig löslich in Wasser und Alkohol, praktisch unlöslich in überschüssiges Nitrat enthaltendem Wasser. (Gef.: Co, 8.90; H_2O, 4.28. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]NO_3,1\frac{1}{2}H_2O$: Co, 8.88; H_2O, 4.07%.)

Saures Sulfat. Rotbraune Nadeln. (Gef.: Co, 8.52; SO_4, 14.40; N, 12.60. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]_2SO_4,H_2SO_4$: Co, 8.77; SO_4, 14.27; N, 12.50%.)

Neutrales Sulfat. Rotbraunes Pulver. (Gef.: Co, 8.32; N, 11.93; H_2O, 11.73. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]_2SO_4,9H_2O$: Co, 8.38; N, 11.94; H_2O, 11.51%.)

Didimethylglyoxim-di-β-naphthylamin-kobalt(III)-salze. *Chlorid.* Gelbe Nadeln. (Gef.: Co. 9.33; H_2O, 2.91. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]Cl,H_2O$: Co, 9.39; H_2O, 2.86%.)

Bromid. Orangefarbene Nadeln. (Gef.: Co, 8.40; H_2O, 8.10. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]Br,3H_2O$: Co, 8:32; H_2O, 7.62%.)

Jodid. Braunes Pulver. (Gef.: Co, 8.38; H_2O, 1.27. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]I,\frac{1}{2}H_2O$: Co, 8.30; H_2O, 1.27%.)

Rhodanid. Braune Prismen. (Gef.: Co, 9.20; H_2O, 1.81. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]SCN,\frac{1}{2}H_2O$: Co, 9.19; H_2O, 1.40%.)

Nitrat. Orangefarbene Nädelchen, ziemlich gut löslich in Wasser. (Gef.: Co, 8.40; H_2O 10.65. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]NO_3,4H_2O$: Co, 8.32; H_2O, 10.15%.)

Saures Sulfat. Orangefarbene Nadeln. (Gef.: Co, 8.60; SO_4, 13.68; N, 11.97; H_2O, 3.41. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]_2SO_4,H_2SO_4,2\frac{1}{2}H_2O$: Co, 8.50; SO_4, 13.80; N, 12.09; H_2O, 3.24%.)

Neutrales Sulfat. Man fällt eine warme Lösung, die auf 10 c.c. Wasser 1 g. des sauren Sulfates enthält, tropfenweise mit etwas weniger der berechneten Menge Natriumkarbonatlösung. Nach dem Erkalten kristallisiert das Salz in gelben Säulen aus. Sehr gut löslich in Wasser. (Gef.: Co, 8.67; H_2O, 9.66. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]_2SO_4,7H_2O$: Co, 8.60; H_2O, 9.18%.)

Freie Base. Erhältlich wie die entsprechende *p*-Toluidinverbindung als schwer lösliche gelbe Schuppen. (Gef.: Co, 9.55; N, 13.69; H_2O, 5.85. Ber. für $[Co(C_{10}H_9N)_2(DH)_2]OH,2H_2O$: Co, 9.40; N, 13.36; H_2O, 5.73%.)

Didimethylglyoxim-di-o-phenylendiamin-kobalt(III)-chlorid. Man trägt in eine Lösung, die auf 30 c.c. Alkohol 1 g. kristallisiertes Kobaltchlorid und 1 g. Dimethylgly-

oxim enthält, 1 g. *o*-Phenylendiamin ein, und oxydiert das Gemisch mit Luft. Das ausgeschiedene Salz wird aus Wasser umkristallisiert. Es bildet in Wasser sehr gut lösliche, schwarzbraune Kristalle. In konzentrierte Schwefelsäure eingeworfen, schäumt es heftig als Kennzeichen eines echten Chlorides. (Gef.: Co, 9.74; N, 18.63; H_2O, 11.89. Ber. für $[Coph_2(DH)_2]Cl,4H_2O$: Co, 9.63; N, 18.30; H_2O, 11.76%.)

Chloro-didimethylglyoxim-*o*-phenylendiamin-kobalt(III). Nach Zusatz von 0.4 g. *o*-Phenylendiamin und 2 c.c. norm. Ätznatron zu 20 c.c. Alkohol, der 1 g. kristallisiertes Kobaltchlorid und 1 g. Dimethylglyoxim gelöst enthält, leitet man in die Lösung sehr lange Luft ein. Die erhaltene Kristalle werden mit etwas Wasser gewaschen und aus Methanol umkristallisiert. Rotbraune Tafeln, schwer löslich in Wasser, ziemlich gut in Alkohol. Reaktion mit konzentrierter Schwefelsäure zeigt, dass das Salz kein ionogenes Chlor enthält. Bei der trockenen Destillation gibt das Destillat die Jodoformreaktion. (Gef.: Co, 12.23; Cl, 7.82; C_2H_5OH, 9.53. Ber. für $[Coph(DH)_2Cl]$, C_2H_5OH: Co, 12.22; Cl, 7.42; C_2H_5OH, 9.61%.)

Didimethylglyoxim-aquo-*o*-phenylendiamin-kobalt(II)-chlorid. Man löst 0.5 g. frisch entwässertes Kobaltchlorid und 1.2 g. Dimethylglyoxim in 20 c.c. völlig wasserfreiem Aceton, fügt dazu 0.4 g. in wenig wasserfreiem Aceton gelöstes *o*-Phenylendiamin. Reibt man einige Zeit die Gefässwand, so scheiden sich gelbe Nadeln mit guter Ausbeute aus, die in Methanol gelöst und unter Zusatz von Äther gefällt werden können. Sehr gut löslich in Alkohol, schwer löslich in Wasser, jedoch mit deutlich saurer Reaktion. Durch Säuren sofort zersetzbar; reagiert mit konzentrierter Schwefelsäure als echtes Chlorid. Mittels der Jodoformreaktion ist Aceton nachweisbar. (Gef.: Co, 10.73; Cl, 12.82; N, 15.33. Ber. für $[Coph(DH_2)_2(OH_2)]Cl_2$, $CH_3{\cdot}CO{\cdot}CH_3$: Co, 10.80; Cl, 13.00; N, 15.36%.)

Zusammenfassung.

Komplexsalze der allgemeinen Formel $[CoA_2(DH)_2]X$, in denen A Ammoniak, Anilin, *o*- und *p*-Toluidin, *m*-Xylidin, bzw. *α*- und *β*-Naphthylamin, und X Cl, Br, J, SCN, NO_3 bzw. $\frac{1}{2}SO_4$ ist, wurden dargestellt. Gleichzeitig wurden einige verwandte Verbindungen dargestellt.

Es wurde gezeigt, dass, wenn *o*-Phenylendiamin als A gebraucht wird, dieses zweiwertige Amin nie als zweizähliger Ligand reagiert, sondern immer einzählig ist, woraus wir schlossen, dass zwei Dimethylglyoximreste in den Komplexsalzen sehr fest plan konfigurieren müssen.

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DIE GESCHWINDIGKEIT DER AUSTAUSCHREAKTION DER WASSERSTOFFATOME ZWISCHEN ZUCKER UND WASSER.

(Vorläufige Mitteilung.)

Von Masao HARADA und Toshizo TITANI.

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Die Austauschbarkeit der H-Atome in den OH-Radikalen von Zucker und Wasser wurde zuerst von Bonhoeffer und Brown entdeckt.(1) Und später wurde das Gleichgewicht dieser Austauschreaktion von Hamill und Freudenberg(2) eingehend untersucht. Ähnliche Versuche führten wir auch aus, um die Verteilung von D-Atomen zwischen einigen Hexosen und schwerem Wasser zu untersuchen. Aber dabei schien es uns notwendig zuerst von der Geschwindigkeit der betreffenden Reaktion Kenntnis zu gewinnen. In dieser Hinsicht haben wir ein Experiment durchgeführt, dessen Ergebnisse wir vorläufig mitteilen wollen.

Zuerst wurde eine Lösung aus 2 bis 3 g. Glukose und 2 g. gewöhnlichem Wasser bzw. 1.5 N H_2SO_4 oder 1.5 N NaOH in einem mit Schliffmündung versehenen Glasrohr hergestellt. Die so bereitete neutrale, sauere oder alkalische Lösung von Glukose wurde dann mit 1 c.c. von 5 prozentigem schweren Wasser versetzt und schnell vermischt. Unmittelbar darauf wurde das Glasrohr mittels des Glasschliffs an einer Vakuumdestillationsanordnung angesetzt, und 50 bis 100 mg. Wasser wurde aus der Lösung in das andere Glasröhrchen schnell abdestilliert. Dazu war durchschnittlich eine Minute erfolderlich. Die so abdestillierte Wasserprobe wurde zur Dichtebestimmung gesondert aufbewahrt. Dann wurde die Abdestillation kleiner Mengen von Wasser aus derselben Lösung drei bis fünf Mal bei verschiedenen Zeiten nach der Vermischung sukzessiv wiederholt. Die letzte Probe wurde entsprechend dem Gleichgewichtszustand mindestens nach 24 Stunden vorgenommen. Die so gesammelten Wasserproben wurden separat je durch zweimalige Destillation gereinigt. Dann wurde ihre Dichte durch die Schwebemethode mittels eines kleinen Glasschwimmers bestimmt und miteinander verglichen.

(1) K. F. Bonhoeffer und G. W. Brown, *Z. physik. Chem.*, B, **23** (1933), 171.
(2) W. H. Hamill und W. Freudenberg, *J. Am. Chem. Soc.*, **57** (1935), 1427.

Aus diesem Experiment ergaben sich die folgenden Tatsachen:

(1). Das Wasser, das innerhalb einer Minute, der kürzesten Zeit die wir erreichen konnten, nach der Vermischung aus der Glukose-Lösung durch die Destillation gewonnen wurde, besass innerhalb des Messfehlers genau dieselbe Dichte wie die des Wassers, das nach mehr als 24 Stunden aus derselben Lösung abdestilliert wurde. Daraus ersieht man sofort, dass das Austauschgleichgewicht zwischen Glukose und Wasser mindestens innerhalb einer Minute erreicht wird.

(2). Wir erhielten immer dasselbe Resultat ohne Unterschied, ob wir die neutrale, sauere oder alkalische Lösung der Glukose benutzten. Daher vermuten wir, dass die Austauschreaktion zwischen Glukose und Wasser sehr schnell vor sich geht.

Wir haben das Experiment auch mit Fruktose durchgeführt. Aber die Resultate erwiesen sich als genau dieselben wie oben. Die eben gefundenen Verhältnisse müssen beim Versuch über das Austauschgleichgewicht zwischen Zucker, oder vermutlich auch anderen ähnlichen organischen Verbindungen, und schwerem Wasser, besonders beim Abtrennen der Verbindungen von Wasser, in Betracht gezogen werden.

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ON THE VISCOSITY OF THE CRITICAL MIXTURE OF TERNARY SYSTEM BENZENE-ALCOHOL-WATER.

By Osamu KIMURA.

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Introduction. It is a well-known phenomenon that a liquid shows critical opalescence at its critical state. Two component system also shows this phenomenon and there are numerous investigations[1] on this problem. The author has studied colloid-chemically on the three component system of organic solvents[2]. The optical method seems to be superior, but from the standpoint of colloid chemistry, the viscometric method is one of the most usefull methods for studying the liquid of colloidal nature. In this paper the viscosity of three component system is measured at its critical state and some discussions concerning the colloidal properties of critical mixture are described.

Experimental. The three component system benzene-ethanol-water has been studied by the author and reported in a previous paper[2]. This system is the most familiar and the materials are easily purified. Recently the viscosity of this system was measured by Pestemer[3], but he paid no attention to the colloidal nature at the critical state. This system shows critical opalescence at a certain temperature and composition, and when the temperature is raised, the intensity of opalescence becomes weak by and by, and at last the opalescence disappears and the total system becomes homogeneous. It must be noticed that this state which shows critical opalescence is very stable and does not change for long time if the temperature is maintained constant. The viscosity has been measured following this stadium at various temperatures. The apparatus used is a modified type of Ostwald viscosimeter, which is shown in Fig. 1.

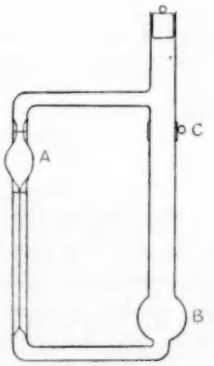


Fig. 1.

Even a slight vaporisation of a component affects the state of the system markedly, so that after pouring the liquid in viscosimeter the inlet tube is

(1) J. Friedländer, *Z. physik. Chem.*, **38** (1901), 435. V. Rothmund, *Z. physik. Chem.*, **63** (1908), 54. Wo. Ostwald, *Ann. Phys.*, (4), **36** (1911), 848.
(2) N. Sata and O. Kimura, this Bulletin, **10** (1935), 409.
(3) M. Pestemer, *Kolloid-Z.*, **65** (1933), 25.

sealed. The total apparatus is dipped in a thermostat, the temperature of which is changeable. To measure the viscosity the apparatus is rotated in left hand, C being the axis of rotation, so that the liquid in B fills the bulb A. Then it is again rotated reversely and the apparatus is fixed vertical. The transpiration time of liquid between two marks is measured by a stopwatch. On the other hand the density of the liquid is measured by Ostwald pycnometer and the viscosity is calculated. The viscosity was measured on five series of different compositions, of which three systems showed critical opalescence, and the other two did not. The compositions of these five systems are shown in Table 1, and graphically in Fig. 2. The temperature is varied from homogeneous domain to the critical point.

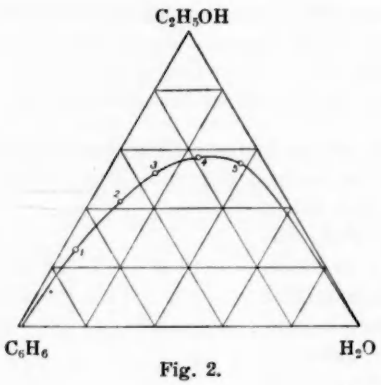


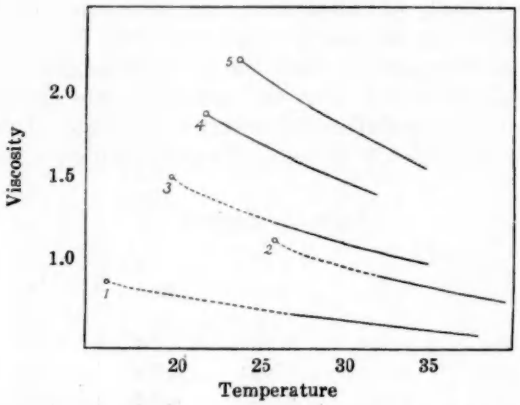
Fig. 2.

Table 1. Compositions of Five Systems in Volume Percent.

System	Benzene	Ethanol	Water	Remarks
1	70 3	26.2	3.5	shows opalescence
2	48.3	42.3	9.4	,,
3	33.7	52.2	14.1	,,
4	18.1	57.6	24.3	no opalescence
5	7.2	55.7	37.1	,,

Results and Discussion. The experimental results are shown graphically in Fig. 3. It is seen that the viscosity-temperature curve has a gentle slope in homogeneous region and a steep one in the region which shows opalescence. This sudden increase of viscosity in critical region was pointed out by Friedländer and Rothmund, but the reason of this increase was not discussed. It may be easily supposed that this sudden increase of viscosity is caused by the existence of colloidal particles which are the small droplets of benzene covered with thin film of alcohol, as was reported in the previous paper. Moreover this conception is confirmed by the experimental data that the viscosity-temperature curve of the system which shows no opalescence (i.e. there is no colloidal region) has gentle slope, while that of the system which shows opalescence is very steep in colloidal region. To show this more quantitatively some considerations have been made.

Concerning viscosity-temperature relation, there are numerous formulas theoretical and empirical. Among these Andrade's formula[4] is an excellent



—— homogeneous region, ------ colloidal region, o critical point

Fig. 3.

one because it is very simple and contains only two constants and furthermore it is applicable to wide range of temperature and many substances. The formula is as follows:

$$\eta = Ae^{b/T},$$

where A and b are constants, and T is the absolute temperature.
The formula was applied to the homogeneous region determining the two constants by means of the least square. The formula is highly applicable to the homogeneous region within the deviation of 0.5%. But when it is extrapolated in the colloidal region, the deviation from calculated values is remarkable and the nearer the critical point the greater the deviations. To the system which shows no opalescence it is applicable up to the critical point. This deviation is, as already explained due to colloidal nature (i.e. emulsion) of the system.

For the viscosity-concentration relation of emulsion Hatschek presented following formula:

(4) C. Andrade, *Nature*, **125** (1930), 309.

$$\eta = \eta_m \frac{1}{1-\sqrt[3]{\phi}},$$

where η is the viscosity of emulsion, η_m that of medium, ϕ the volume of dispersed phase in unit volume of emulsion. This formula was verified experimentally by many investigators, and among those Sibree[5] has carefully measured the viscosity of emulsions and concluded that Hatschek's formula is applicable to many types of emulsion very satisfactorily if not strictly. If this formula can be applied to this case, the concentration of emulsion is cal-

Table 2. System 1.

°C.	t (sec.)	d	$\eta_{obs.}$	$\eta_{calc.}$	$\Delta\eta$	ϕ
38.0	54.3	0.8403	0.5836	0.5836	0.0000	
37.0	55.2	0.8413	0.5940	0.5931	+0.0009	
36.0	55.9	0.8422	0.6021	0.6028	−0.0007	
35.0	56.7	0.8432	0.6115	0.6129	−0.0014	
34.0	57.7	0.8441	0.6229	0.6230	−0.0001	
33.0	58.7	0.8451	0.6345	0.6334	+0.0009	
32.0	59.5	0.8461	0.6438	0.6450	−0.0012	
31.0	60.5	0.8470	0.6554	0.6551	+0.0003	
30.0	61.5	0.8479	0.6670	0.6662	+0.0008	
29.0	62.5	0.8489	0.6786	0.6784	+0.0002	
28.0	63.5	0.8498	0.6902	0.6896	+0.0006	
27.0	64.5	0.8508	0.7002	0.7017	−0.0015	
26.0	65.5	0.8517	0.7135	0.7140	0.0005	0.000005
25.0	67.0	0.8527	0.7307	0.7265	0.0042	0.00004
24.0	68.0	0.8536	0.7414	0.7390	0.0024	0.00002
23.0	69.3	0.8546	0.7574	0.7527	0.0047	0.00005
22.0	70.8	0.8556	0.7747	0.7662	0.0085	0.00009
21.0	72.2	0.8565	0.7909	0.7802	0.0107	0.00011
20.0	73.7	0.8575	0.8083	0.7945	0.0138	0.00014
19.0	75.0	0.8584	0.8234	0.8090	0.0144	0.00014
18.0	76.5	0.8594	0.8409	0.8241	0.0168	0.00017
17.0	78.4	0.8603	0.8626	0.8393	0.0233	0.00023
16.3	79.6	0.8610	0.8765	0.8504	0.0261	0.00026
16.0	critical point					

(5) J. O. Sibree, *Trans. Faraday Soc.*, **26** (1930), 104; **27** (1931), 161.

Table 3. System 2.

°C.	t (sec.)	d	$\eta_{obs.}$	$\eta_{calc.}$	$\Delta\eta_i$	ϕ
40.0	71.4	0.8398	0.7669	0.7673	−0.0004	
39.0	73.0	0.8408	0.7850	0.7852	−0.0002	
38.0	74.7	0.8418	0.8042	0.8037	+0.0005	
37.0	76.3	0.8428	0.8224	0.8227	−0.0003	
36.0	78.1	0.8439	0.8430	0.8422	+0.0008	
35.0	79.7	0.8449	0.8613	0.8627	−0.0014	
34.0	81.7	0.8459	0.8839	0.8834	+0.0005	
33.0	83.6	0.8469	0.9055	0.9048	+0.0007	
32.0	85.5	0.8479	0.9272	0.9272	+0.0000	
31.0	88.0	0.8489	0.9554	0.9500	+0.0054	0.0000001
30.0	91.4	0.8499	0.9935	0.9734	+0.0201	0.0000087
29.0	93.1	0.8510	1.012	0.9993	+0.013	0.0000022
28.0	95.8	0.8520	1.044	1.023	+0.011	0.0000013
27.0	99.0	0.8530	1.080	1.049	+0.031	0.000026
26.0	103.8	0.8540	1.134	1.076	+0.058	0.00016
25.0	critical point					

Table 4. System 3.

°C.	t (sec.)	d	$\eta_{obs.}$	$\eta_{calc.}$	$\Delta\eta_i$	ϕ
35.0	92.4	0.8451	0.9987	0.9992	−0.001	
34.0	94.4	0.8461	1.022	1.022	0.000	
33.0	96.6	0.8471	1.047	1.046	+0.001	
32.0	98.7	0.8481	1.071	1.071	0.000	
31.0	101.0	0.8491	1.097	1.097	0.000	
30.0	103.2	0.8501	1.122	1.123	−0.001	
29.0	105.7	0.8511	1.151	1.151	0.000	
28.0	108.2	0.8521	1.176	1.178	−0.002	
27.0	110.8	0.8531	1.209	1.207	+0.002	
26.0	113.4	0.8541	1.239	1.236	+0.003	
25.0	116.8	0.8551	1.277	1.267	+0.010	0.0000005
24.0	120.0	0.8560	1.314	1.297	+0.017	0.000002
23.0	123.2	0.8570	1.350	1.331	+0.019	0.000003
22.0	126.7	0.8580	1.390	1.364	+0.026	0.000007
21.0	130.4	0.8589	1.432	1.399	+0.033	0.000013
20.0	136.8	0.8599	1.505	1.435	+0.070	0.000116
19.5	critical point					

Table 5. System 4.

°C.	t (sec.)	d	$\eta_{obs.}$	$\eta_{calc.}$	$\Delta\eta$
32.0	126.7	0.8646	1.401	1.401	0.000
31.0	130.3	0.8655	1.442	1.440	+0.002
30.0	134.0	0.8664	1.485	1.481	+0.004
29.0	137.4	0.8673	1.524	1.526	−0.002
28.0	141.1	0.8682	1.567	1.567	0.000
27.0	145.1	0.8691	1.613	1.613	0.000
26.0	148.9	0.8700	1.657	1.660	−0.003
25.0	153.3	0.8709	1.708	1.709	−0.001
24.0	157.7	0.8718	1.758	1.757	+0.001
23.0	162.2	0.8727	1.811	1.811	0.000
22.0	167.0	0.8736	1.866	1.866	0.000
21.0	critical point				

Table 6. System 5.

°C.	t (sec.)	d	$\eta_{obs.}$	$\eta_{calc.}$	$\Delta\eta$
35.0	136.0	0.8917	1.551	1.555	−0.004
34.0	140.0	0.8925	1.598	1.601	−0.003
33.0	144.4	0.8934	1.650	1.651	−0.001
32.0	149.0	0.8943	1.704	1.700	+0.004
31.0	153.2	0.8952	1.754	1.752	+0.002
30.0	157.6	0.8960	1.806	1.805	+0.001
29.0	162.1	0.8969	1.859	1.865	−0.006
28.0	166.8	0.8977	1.915	1.920	−0.005
27.0	172.4	0.8986	1.981	1.980	+0.001
26.0	177.2	0.8994	2.038	2.043	−0.005
25.0	183.2	0.9003	2.110	2.108	+0.003
24.0	189.3	0.9012	2.182	2.173	+0.009
23.0	critical point				

culated as follows. In the formula η is the viscosity of emulsion which is the observed viscosity in this case, and η_m is the viscosity of medium, which can be calculated from Andrade's formula. Then we obtain

$$\phi = \left(\frac{\eta - \eta_m}{\eta}\right)^3 = \left(\frac{\Delta\eta}{\eta}\right)^3.$$

Thus the values of ϕ were calculated for three systems which showed critical opalescence. These values are illustrated in Table 2, 3, 4, 5, and 6. In the tables the 1st column is the temperature in centigrade, the 2nd the time of transpiration between two marks, the 3rd the density, the 4th the observed viscosity, in centipoise, the 5th the viscosity calculated by using Andrade's formula, the 6th the difference between observed and calculated viscosities, and the 7th the concentration calculated from Hatschek's formula.

It is seen from the tables that the concentration of colloid particles which are supposed to be the droplets of benzene covered with thin film of alcohol is of the order of 0.0001 near the critical point and decreases as the temperature is raised. There may be some relations between the concentration and the intensity of opalescence, which also shows maximum at critical point and decreases as the temperature is raised. The experiment on this line is now in course.

Summary.

(1) The viscosity of the three component system benzene-ethanol-water was measured in the neighbourhood of critical point.

(2) To the homogeneous region Andrade's formula is strictly applicable but not to the colloidal region. This deviation is caused by the existence of colloid particles.

(3) The concentration of colloid particles was calculated by using Hatschek's formula, and it was of the order of 0.0001 near the critical point.

The author expresses his sincere thanks to Prof. N. Sata, at whose suggestion this work has been carried out.

The Shiomi Institute of Physical and Chemical Research.

A VISCOSITY FORMULA FOR BINARY MIXTURES, THE ASSOCIATION DEGREES OF CONSTITUENTS BEING TAKEN INTO CONSIDERATION. SUMMARY.

By Tetsuya ISHIKAWA and Toshitomo BABA.

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The probable values of the normal K relative to that of benzene. Before closing this series of the viscosity study,[1] we will consult as much as available data found in the literature in order to have the probable values of the normal K.

Mixtures adopted here are (1) those the viscosity curves of which are convex or quite rarely concave towards the composition axis, and (2) these both component K's of which in accord with Ishikawa's theory have already been known, although they indicate viscosity maxima or minima.

The following notations will be used:

K signifies the ratio of the characteristic constant (ka) of component 2 to that of component 1 in formula (1) for chemically indifferent mixtures:

$$\eta = \frac{\eta_1}{1+K\frac{z_m}{1-z_m}} + \frac{\eta_2}{1+\frac{1}{K}\frac{1-z_m}{z_m}} \qquad (1).$$

This normal case is simply denoted by the symbol n.

In the course of the calculation we have met with cases in which K's slightly vary as concentration, and either of the extrapolated values of K at $z_m = 0$ or $z_m = 1$ if taken much differs from the probable value of the normal K. Such anomaly is observed in the following mixtures: Acetone—*i*-propyl alcohol, carbon tetrachloride—tetrachloroethane, &c. However, further tests for these mixtures prove that they must be classified into the following case.

K' and K'' denote the ratios of the characteristic constant (ka) of component 2 to that of component 1 and that of component 1 to that of component 2 respectively, more or less differing from K and $1/K$ in formula (1) or $K'K'' > 1$ as a result of anomalous changes in molecular association:

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(1) This Bulletin, **4** (1929), 5, 25, 149, 288; **5** (1930), 47, 117; **8** (1933), 280, 293; **9** (1934), 155; **10** (1935), 153, 248; **11** (1936), 8.

$$\eta = \frac{\eta_1}{1+K'\dfrac{z_m}{1-z_m}} + \frac{\eta_2}{1+K''\dfrac{1-z_m}{z_m}} \qquad (2).$$

This formula for anomalous change in association on mixing holds true for the concentration range between the two extremities close to $z_m = 0$ and $z_m = 1$, where the numbers of molecules of one component become quite enough to change its original association into some other associations statistically at extremely low concentration and at extremely high concentration diluted with the other component. This anomalous case is abbreviated by the symbol a.

For the case in which the association degree of a component varies as dilution with the other, the extrapolated value of K at $z_m = 0$ or $z_m = 1$ gives the normal K for the mixture. The mixtures of phenol, guaiacol, or benzyl benzoate with benzene or toluene in which the former components suffer molecular dissociation are examples of this case. The formulation of the viscosity–composition curves of such mixtures cannot be generally done, since the decreasing rate of the association degree with dilution depends upon its own peculiarity of the associated component against the solventing action of the other component, yet a particular case can be solved with a particular means, say, taking K or its reciprocal at each composition for test whether they are in a linear relationship with composition or not. This variable case (3) is briefly denoted by the symbol v, and both extrapolated values at $z_m = 0$ and $z_m = 1$ are written thus: e.g. 0.087–0.227 for C_6H_6 (1)–C_6H_5OH (2).

The mixture phenol–dimethylaniline is considered as one more example of the case. The viscosity–composition curves observed by Bramley at the temperatures between 10° and 180°C. are sinuous nature as seen from Fig. 1 in which the points are the observed viscosities. Simply judging from the curves, one may imagine, as Bramley does, that the mixture appears to have a compound, but the freezing-point curve consists of two branches only, the eutectic temperature being found to be −36.0°C. according to Bramley.[2] Once when we take, however, K as ordinate and z_m as abscissa, we readily see that the points at each temperature lie on a straight line. This fact shows that there occurs the molecular dissociation of phenol but no molecular compound just as the freezing-point diagram requires. The curves in Fig. 1 are traced on thus calculated viscosities (see Table 1).

(2) A. Bramley, *J. Chem. Soc.*, **109** (1916), 469.

Table 1. Phenol—Dimethylaniline, (Bramley).

z_m	10°C.		z_m	29.8°C.		59.9°C.	
	$\gamma_{obs.}$	$\gamma_{calc.}$		$\gamma_{obs.}$	$\gamma_{calc.}$	$\gamma_{obs.}$	$\gamma_{calc.}$
0.0000	0.2010	—	0.0000	0.0709	—	0.02530	—
0.0571	0.1964	0.1946	0.0537	0.0686	0.0687	0.02665	0.02473
0.1173	0.1850	0.1801	0.1116	0.0648	0.0650	0.02380	0.02387
0.1785	0.1639	0.1596	0.1726	0.06025	0.06003	0.02270	0.02274
0.2500	0.1347	0.1327	0.2409	0.05325	0.05352	0.02100	0.02124
0.3149	0.1094	0.1092	0.3046	0.04705	0.04721	0.01960	0.01972
0.3815	0.0869	0.0881	0.3778	0.0393	0.04025	0.01760	0.01790
0.4542	0.0696	0.0693	0.4452	0.0333	0.03448	0.01587	0.01627
0.5340	0.05315	0.0535	0.5231	0.0283	0.02373	0.01428	0.01451
0.6110	0.04185	0.0421	0.6151	0.02315	0.02335	0.01267	0.01268
0.7115	0.03145	0.0317	0.7042	0.01936	0.01928	0.01123	0.01118
0.7879	0.02586	0.0259	0.7960	0.01629	0.01616	0.01001	0.00992
0.8861	0.02076	0.0207	0.9001	0.01351	0.01356	0.00878	0.00881
1.0000	0.01654	—	1.0000	0.01173	—	0.00799	—
	$K = 0.25+6.05\ z_m$.			$K = 0.50+3.36\ z_m$.		$K = 0.50+1.93\ z_m$.	

Table 2. Acetone—Phenol, (Bramley).

z_m	9.95°C.		20.05°C.	
	$\gamma_{obs.}$	$\gamma_{calc.}$	$\gamma_{obs.}$	$\gamma_{calc.}$
0.0000	0.00360	—	0.00323	—
0.0926	0.00486	0.00486	0.00429	0.00432
0.1837	0.00635	0.00636	0.00560	0.00559
0.2749	0.00868	0.00873	0.00755	0.00752
0.3761	0.01256	0.01265	0.01055	0.01061
0.4580	0.01688	0.01683	0.01379	0.01402
0.5363	0.02358	0.02338	0.01853	0.01828
0.6340	0.03670	0.03722	0.02750	0.0273
0.6982	0.0495	0.0501	0.0359	0.0357
0.7829	0.0748	0.0736	0.0497	0.0500
0.8890	0.1193	0.1194	0.0730	0.0745
1.0000	0.2010	—	0.1104	—
	$K = 0.063$ ($z_m = 0.0$–0.20); $K = 0.0485+0.079\ z_m$ ($z_m = 0.20$–0.55); $K = -0.026+0.228\ z_m$ ($z_m = 0.55$–1.0).		$K = 0.100$ ($z_m = 0.0$–0.20); $K = 0.077+0.120\ z_m$ ($z_m = 0.20$–0.55); $K = -0.033+0.316\ z_m$ ($z_m = 0.55$–1.0).	

Table 2. (*Concluded*)

z_m	29.8°C.		40.1°C.		49.8°C.	
	$\eta_{obs.}$	$\eta_{calc.}$	$\eta_{obs.}$	$\eta_{calc.}$	$\eta_{obs.}$	$\eta_{calc.}$
0.0000	0.002950	—	0.002700	—	0.002480	—
0.0613	0.003599	0.003596	0.003279	0.003273	0.002990	0.002980
0.1302	0.004409	0.004414	0.003991	0.003987	0.003599	0.003604
0.1912	0.005212	0.005233	0.004700	0.004698	0.004219	0.004216
0.2695	0.00670	0.00656	0.005899	0.005756	0.005299	0.005133
0.3324	0.00808	0.00805	0.00711	0.00698	0.006281	0.006177
0.4179	0.01058	0.01065	0.00904	0.00908	0.00794	0.00794
0.4832	0.01319	0.01321	0.01101	0.01105	0.00950	0.00956
0.5581	0.01658	0.01682	0.01362	0.01384	0.01149	0.01175
0.6401	0.02179	0.02188	0.01742	0.01759	0.01425	0.01459
0.7213	0.02747	0.02838	0.02232	0.02219	0.01786	0.01768
0.8187	0.03922	0.03886	0.02874	0.02911	0.02247	0.02246
0.8880	0.04902	0.04873	0.03460	0.03516	0.02618	0.02615
1.0000	0.07092	—	0.04739	—	0.03279	—
	$K = 0.147$ ($z_m = 0.0$–0.20); $K = 0.105+0.175\,z_m$ ($z_m = 0.20$–1.0).		$K = 0.198$ ($z_m = 0.0$–0.20); $K = 0.140+0.220\,z_m$ ($z_m = 0.20$–1.0).		$K = 0.257$ ($z_m = 0.0$–0.20); $K = 0.177+0.308\,z_m$ ($z_m = 0.20$–1.0).	

Another example of this case in which K sometimes occurs to be composed of two or more sets of linear functions of z_m suggests the molecular dissociation of one component in two or more stages. For a good example the mixture of phenol (2) with acetone (1) measured by Bramley will be adopted here. Fig. 2 shows the K's plotted against the composition, in which we make distinct classifications of the points in three sets of straight lines at 10° and 20°C., and in two sets at 30° and higher temperatures. In Table 2 $\eta_{calc.}$ are obtained by assuming these sets of linear relationship of K with composition. As judged from the numerical values of the cutting points of the elongations of these sets of lines at each temperature at phenol-pure axis, the degradation of phenol-associated molecules is well explained if we assume that the phenol in its pure state consists mainly of trimol at low temperatures and of dimol at high temperatures; that is, of the three sets at low temperatures the first phenol-rich set indicates the coexistence of trimol and dimol, the second the coexistence of dimol and monomol, and the third the existence of monomol only, whereas at higher temperatures the first set at phenol-rich solutions shows the coexistence of dimol and monomol, and the second the existence of monomol only, all in equilibrium with acetone molecules. The above elucida-

tion, though it indicates no appreciable presence of a molecular compound, yet the presence of dynamic equilibrium of dimol and monomol whose relative

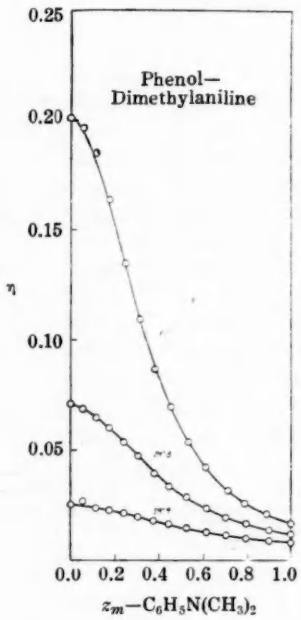

Fig. 1.

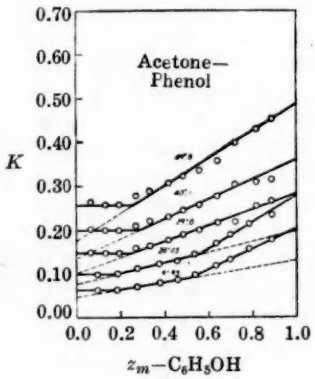

Fig. 2.

amounts to each other are nearly independent of temperature, is affirmative to the melting-point diagram observed by Schmidlin and Lang[3] which records a greatly dissociated molecular compound $(CH_3)_2CO \cdot 2C_6H_5OH$ melting at 15°C.

ν_1 and ν_2 signify the molecular numbers of components 1 and 2 in the molecular compound in accord with formula (4):

$$\eta = \frac{\eta_1}{1+K\frac{z_m}{1-z_m}} + \frac{\eta_2}{1+\frac{1}{K}\frac{1-z_m}{z_m}} + C_0(\eta_1^{\nu_1}\eta_2^{\nu_2})^{\frac{m}{\nu_1+\nu_2}}(1-z_m)^{\nu_1} z_m^{\nu_2} \qquad (4),$$

where C_0 and m are constants independent of the temperature and concentration. This case in which a compound occurs is denoted by the symbol c (ν_1 : ν_2).

(3) J. Schmidlin and R. Lang, *Ber.*, **43** (1910), 2812.

An interesting system for case (4) is the water−pyridine mixture. The solvation viscosity $\delta=\eta-\eta_0$ of this mixture at 0° and 25°C. appears to consist of two terms up to 30 mol % pyridine, i.e. it is not simply proportional to $(1-z_m)^3z_m$ or $(1-z_m)^2z_m$, but it corresponds to the sum of some or other

Table 3. Water−Pyridine, (Hartley, Thomas, and Applebey).

0°C.

z_m	η	η_0	δ	$\delta_{calc.}$		$\eta_{calc.}$
0.0000	0.01778	—				—
0.0236	0.02448	0.01765	0.00683	0.00672		0.02437
0.0564	0.03218	0.01747	1471	1482		0.03229
0.0872	0.03840	0.01730	2110	2122		0.03852
0.1306	0.04548	0.01707	2841	2825	$0.104(1-z_m)^3z_m$	0.04532
0.1847	0.05147	0.01679	3468	3461	$+0.197(1-z_m)^2z_m$	0.05140
0.2483	0.05521	0.01646	3875	3860		0.05506
0.2713	0.05562	0.01635	3927	3929		0.05564
0.2985	0.05560	0.01621	3939	3965		0.05586
0.3462	0.05416	0.01598	3818	3806		0.05404
0.4159	0.04905	0.01564	3341	3309		0.04873
0.4780	0.04262	0.01535	2727	2766		0.04301
0.5789	0.03298	0.01489	1899	1844	$0.370(1-z_m)^3z_m$	0.03333
0.6746	0.02398	0.01446	952	1080	$+0.01(1-z_m)z_m$	0.02526
0.8159	0.01729	0.01385	344	338		0.01723
0.9117	0.01463	0.01346	117	103		0.01449
1.0000	0.01321	—				—

$K = 1.19.$

25°C.

z_m	η	η_0	δ	$\delta_{calc.}$		$\eta_{calc.}$
0.0000	0.00890	—				—
0.0240	0.01116	0.00890	0.00226	0.00222		0.01112
0.0515	0.01336	0.00890	446	446		0.01336
0.0890	0.01598	0.00890	708	705		0.01595
0.1312	0.01833	0.00889	944	936	$0.0232(1-z_m)^3z_m$	0.01825
0.1840	0.02032	0.00889	1143	1142	$+0.0743(1-z_m)^2z_m$	0.02031
0.2522	0.02187	0.00889	1298	1293		0.02182
0.3127	0.02225	0.00888	1337	1334		0.02222
0.3450	0.02186	0.00888	1298	1318		0.02206
0.4780	0.01894	0.00887	1007	994		0.01881
0.6730	0.01350	0.00887	463	447		0.01334
0.8126	0.01064	0.00886	178	180	$0.118(1-z_m)^3z_m$	0.01066
0.8864	0.00979	0.00886	93	92	$+0.0077(1-z_m)z_m$	0.00978
0.9186	0.00942	0.00885	57	64		0.00949
0.9576	0.00917	0.00885	32	32		0.00917
1.0000	0.00885	—				—

$K = 1.19.$

multiples of these concentration factors, which phenomenon undoubtedly shows the coexistence of $C_5H_5N \cdot 3H_2O$ and $C_5H_5N \cdot 2H_2O$ in solution for the concentration range. For higher concentrations up to more than 90 mol % pyridine a set of hydrates $C_5H_5N \cdot 3H_2O$ and $C_5H_5N \cdot H_2O$ exists, of which the former greatly predominates, but the dihydrate disappears.

Baud[4] has determined the freezing points of the system but found no decisive hydrates owing to the existence of hidden maxima. He also points out that the volume contraction maximum occurs at 30 mol % pyridine corresponding to $C_5H_5N \cdot 2.3H_2O$, whereas Pariselle[5] has observed that the density maxima at 17° and 25°C. correspond to $C_5H_5N \cdot 3H_2O$ and $C_5H_5N \cdot 3.3H_2O$ respectively. However, if we consider the volume contraction per gram at 0°, 25°, and 50°C. from the density measurements done by Faust,[6] the points of maximum at these temperatures nearly lie at the same composition probably corresponding to $C_5H_5N \cdot 2.3H_2O$. These results may be fairly understood from the present study that the two hydrates $C_5H_5N \cdot 3H_2O$ and $C_5H_5N \cdot 2H_2O$ coexist in solution, and the former is more stable than the latter as clearly recognized from the concentration ranges of their existence (see Table 3) and also from the amounts of m, the stability coefficient, of these compounds, m of the former being estimated to be 2.4 up to 30 mol % and 1.8 up to more than 90 mol % or in the mean 2.1, while m of the latter to be 1.6 between 0 and 30 mol %.

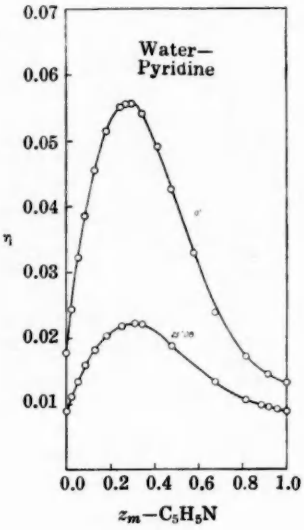

Fig. 3.

Fig. 3 shows how the theoretical and observed viscosities compare graphically.

It rarely happens that anomalous change occurs in association and thence follows a further chemical change to form a molecular compound. For such a case, the formula in combination of formula (2) with the second term of formula (4) may suffice to express the nature of the viscosity—composition curve. Mixtures as that of formamide with *i*-butyl alcohol or with *i*-amyl

(4) E. Baud, *Bull. soc. chim.*, [4], **5** (1909), 1022.
(5) Pariselle, *Compt. rend.*, **172** (1921), 673.
(6) O. Faust, *Z. physik. Chem.*, **79** (1912), 104.

alcohol where both a maximum and a minimum display themselves at low temperatures belong to this case:

$$\eta = \frac{\eta_1}{1+K'\dfrac{z_m}{1-z_m}} + \frac{\eta_2}{1+K''\dfrac{1-z_m}{z_m}} + C_0(\eta_1^{\nu_1}\eta_2^{\nu_2})^{\frac{m}{\nu_1+\nu_2}}(1-z_m)^{\nu_1}z_m^{\nu_2} \qquad (5).$$

The calculation by this formula which appears to be difficult will become easy, if we remember that K' or K'' is often nearly equivalent to K or its reciprocal as in the mixtures of higher alcohols with benzene, together with the presupposition for the values ν_1 and ν_2 from the position of a maximum point in the actual curve. For example, the mixture of *i*-amyl alcohol (1) and formamide (2) as determined by Drucker and Kassel will be considered in the following. Since K of formamide is 0.34 and that of *i*-amyl alcohol is nearly 0.30 as supposed from K (0.29) of γ-amyl alcohol, the probable value for K in this mixture may be nearly 1.17 at an extremity. From the maximum points of the viscosity curves at 0° and 76.5°C., the case for which $\nu_1 = 1$ and $\nu_2 = 2$ is highly probable. After a few trials we have the following equations which are good enough to represent the nature of the curves:

$$\eta = \frac{0.0883}{1+1.77\dfrac{z_m}{1-z_m}} + \frac{0.0755}{1+1.1\dfrac{1-z_m}{z_m}} + 0.287(1-z_m)z_m^2 \quad \text{at} \quad 0°\text{C.},$$

$$\eta = \frac{0.00951}{1+1.1\dfrac{z_m}{1-z_m}} + \frac{0.01255}{1+1.1\dfrac{1-z_m}{z_m}} + 0.0128(1-z_m)z_m^2 \quad \text{at} \quad 76.5°\text{C.}$$

The calculated viscosities show no functional divergence from the observed viscosities as seen from Table 4 and also Fig. 4 in which the curves are drawn with the calculated values.

Peculiar systems for which the viscosity maxima often display themselves as hundreds times greater than the component viscosities are also understood as special cases of formula (4).

Acetic acid—stannic chloride and ethyl formate—stannic chloride are good examples of such cases. For the former pair a molecular compound $SnCl_4 \cdot 3CH_3COOH$ is pointed out by Stranathan and Strong with the viscosity courves the maximum points of which exactly correspond to this molecular ratio, probably independent of temperature. For the latter pair a molecular compound $SnCl_4 \cdot 2HCO_2C_2H_5$ has been confirmed by Kurnakow from the measurements of the viscosities at 30°, 40°, and 50°C. and of the fusion curve.

Table 4. *i*-Amyl alcohol—Formamide, (Drucker and Kassel).

z_m	0°C.		76.5°C.	
	$\eta_{obs.}$	$\eta_{calc.}$	$\eta_{obs.}$	$\eta_{calc.}$
0.0000	0.0883	—	0.00951	—
0.0538	0.0848	0.0848	0.00966	0.00960
0.1783	0.0836	0.0837	0.01005	0.01008
0.4571	0.0992	0.1008	0.01178	0.01183
0.6633	0.1111	0.1106	0.01311	0.01295
0.8194	0.1064	0.1053	0.01322	0.01324
0.9441	0.0858	0.0881	0.01292	0.01292
1.0000	0.0755	—	0.01255	—

Since the viscosities of both components in this type of mixtures are negligibly small as compared to the viscosity of the solution, the consideration of the true value of K is not useful for the approximate estimation of ν_1 and ν_2 in formula (4). In the following calculation, therefore, viscosity deviations are taken from formula (1) in which K is put as unity.

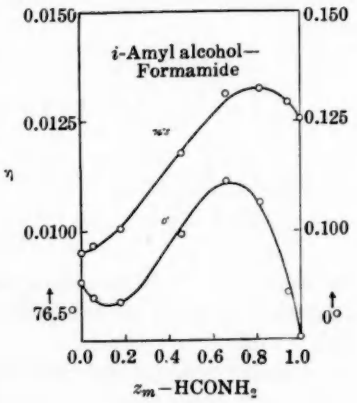

Fig. 4.

As clearly indicated in Table 5, a molecular compound $SnCl_4 \cdot 3CH_3COOH$ exists as some multiple of the simplest molecular ratio, 2-fold up to 5 mol %, 7-fold up to 17 mol %, and 14-fold for higher concentrations.

Similar phenomena are also seen from Table 6 for the mixture of ethyl formate and stannic chloride. In this mixture a molecular compound $SnCl_4 \cdot 2HCO_2C_2H_5$ exists as a great molecule of 30-fold of the simplest ratio at concentrations up to ca 36 mol % at 30°, 40°, and 50°C., but exists as a greater molecule of 60-fold at the concentration range from 32 to 36 mol % at 30°C., under which temperature an enormous crystallization of this compound begins, the melting point of it, however, being at 49°C. according to the same observer.

One more molecular compound $SnCl_4 \cdot HCO_2C_2H_5$ may probably exist at ca 7-fold of the simplest ratio, though the constancy of $\delta/\{(1-z_m)z_m\}^{\nu}$ is not sufficiently good.

These studies suggest that the multiple number of the simplest ratio of a molecular compound at sufficiently low temperature as crystallization begins may be in close relationship with the crystal structure or probably with the dimension of the secondary structure of a crystal as judged from the magnitude of thus estimated multiple of the supposed molecular volume of the molecular compound.(7)

Table 5. Acetic acid—Stannic chloride, 25.2°C., (Stranathan and Strong).

z_m	η	δ	$\delta/(1-z_m)^{\nu_1} z_m^{\nu_2}$		
0.0000	0.01155				
0.0244	0.02121	0.00974	19.0	mean 17.7	$\nu_1 = 3\times2$, $\nu_2 = 1\times2$.
0.0520	0.04373	0.03234	16.4		
0.1084	0.1897	0.1785	1.13×10^7	mean 1.13×10^7	$\nu_1 = 3\times7$, $\nu_2 = 1\times7$.
0.1719	0.963	0.952	1.13×10^7 (1.33×10^{14})		
0.2290	2.582	2.571	1.30×10^{14}	mean 1.42×10^{14}	$\nu_1 = 3\times14$, $\nu_2 = 1\times14$.
0.2527	3.034	3.023	1.44 ,,		
0.2682	2.909	2.898	1.44 ,,		
0.2969	2.105	2.094	1.34 ,,		
0.3151	1.649	1.638	1.42 ,,		
0.3498	0.864	0.854	1.45 ,,		
0.3608	0.691	0.681	1.57 ,,		
0.4111	0.4234	0.4131	(4.75 ,,)		
1.0000	0.0084				

Table 6. Ethyl formate—Stannic chloride, (Kurnakow).

30°C.

z_m	η	δ	$\delta/(1-z_m)^{\nu_1} z_m^{\nu_2}$		
0.00	0.00375				
0.25	0.08788	0.08305	2.99×10^{24}	mean 2.96×10^{24}	$\nu_1 = 2\times30$, $\nu_2 = 1\times30$.
0.30	0.31158	0.30654	2.93 ,,		
0.32	0.52286	0.51773	3.22×10^{49}	3.28×10^{49}	$\nu_1 = 2\times60$, $\nu_2 = 1\times60$.
0.335	0.57832	0.57313	3.33 ,,		
0.36	0.44142	0.43612	3.29 ,,		
0.50	0.06871	0.06281	1.03×10^3	1.03×10^3	$\nu_1 = 1\times7$, $\nu_2 = 1\times7$.
0.75	0.01526	0.00828	1.02 ,,		
1.00	0.00806				

(7) This Bulletin, **10** (1935), 248.

Table 6. (*Concluded*)

40°C.

z_m	η_i	δ	$\delta/(1-z_m)^{\nu_1} z_m^{\nu_2}$	
0.00	0.00342			
0.25	0.06384	0.05946	2.14×10^{24}	
0.30	0.19034	0.18577	1.78 ,,	mean 2.05×10^{24}
0.32	0.27615	0.27150	2.14 ,,	$\nu_1 = 2\times30$, $\nu_2 = 1\times30$.
0.335	0.29541	0.29071	2.22 ,,	
0.36	0.23514	0.23034	2.00 ,,	
0.50	0.04952	0.04419	7.2×10^{2}	7.7×10^{2} $\nu_1 = 1\times 7$,
0.75	0.01292	0.00663	8.1 ,,	$\nu_2 = 1\times 7$.
1.00	0.00725			

50°C.

z_m	η_i	δ	$\delta/(1-z_m)^{\nu_1} z_m^{\nu_2}$	
0.00	0.00311			
0.25	0.04904	0.04504	1.62×10^{24}	
0.30	0.12463	0.12045	1.15 ,,	mean 1.29×10^{24}
0.32	0.16102	0.15667	1.24 ,,	$\nu_1 = 2\times30$, $\nu_2 = 1\times30$.
0.335	0.16758	0.16327	1.24 ,,	
0.36	0.14237	0.13798	1.20 ,,	
0.50	0.03753	0.03264	5.3×10^{2}	5.9×10^{2} $\nu_1 = 1\times 7$,
0.75	0.01115	0.00536	6.5 ,,	$\nu_2 = 1\times 7$.
1.00	0.00668			

General Conclusions. The validity of the above formulas is acknowledged from a great deal of calculations already made (see Table 8). It may fairly be said that formula (1) deserves to be an ideal mixture law which has long been aimed at. The consideration of the viscosity deviation from the ideal mixture law in case where viscosity exhibits a maximum, which idea was introduced by Findlay[8] and by Denision[9] but failed owing to the lack of the true law of ideal mixtures, proves to be true in our case not only in determining the composition of a molecular compound but also in estimating its stability in solution.

The second term of formula (4) or (5) contains two factors, one being concentration function $(1-z_m)^{\nu_1} z_m^{\nu_2}$, the other main corresponding to the viscosity of a molecular compound. One may readily understand that the former is at once deduced from the law of probability by considering the

(8) A. Findlay, *Z. physik. Chem.*, **69** (1909), 203.
(9) R. B. Denison, *Trans. Faraday Soc.*, **8** (1912), 20.

number of encounter between reacting molecules, but one may throw doubt on the form of the latter in which C_0 is independent of concentration and temperature; that is, formula (4) or (5) the second term of which appears to superpose on the first term with respect to composition cannot be elucidative by the classical treatment of chemical equilibrium. If the viscosity of liquids is defined by $\frac{cm\nu}{\sigma}$ as Andrade[10] proposes where m is a mass of a molecule, σ the distance between the centres of molecules, ν the vibration frequency, and c a constant, the number of molecular encounter or collision is proportional to $\frac{\nu}{\sigma}$ which is of the order of some 10^{20} per second. Although the collision probability between ν_1 molecules of kind 1 and ν_2 molecules of kind 2 to form a molecular compound is much less than this amount, the time of such encounter may be beyond comparison with the time ordinarily required for viscosity measurements, so long as a molecular compound is only statistically recognized as such the component molecules of which are freely interchangable with the same kinds of molecules outside of its reaction sphere. Hence the fact that the viscosity of chemically reactive mixtures strictly obeys formula (4) or (5) leads to the conception that a molecular compound is not a fast-combined molecule but a molecular grouping in a statistical meaning.

Formula (4) when applied to the viscosity which exhibits a very marked maximum at low temperature may afford a clue to the study on the mechanism of crystal formation.

Formula (1) is also valid for ideal solutions of solids in liquids.

For a strong electrolyte solution (i) where there occurs no solvation or hydration, the viscosity difference (η^{**}) between the observed specific viscosity (η^{*}) and the viscosity caused by the inter-ionic forces according to the Falkenhagen—Vernon theory[11] obeys formula (1) as expressed in specific quantity:

$$\left.\begin{aligned} \eta^{**} &= 1+\frac{(H-1)Kz_m}{1-z_m+Kz_m} \\ \text{or}\qquad \eta^{*} &= 1+A\sqrt{\frac{1000sz_m}{M_1+(M_2-M_1)z_m}}+\frac{(H-1)Kz_m}{1-z_m+Kz_m} \\ \text{or}\qquad \eta^{*} &= 1+A\sqrt{c}+\frac{(H-1)KM_1c}{1000s+(KM_1-M_2)c} \end{aligned}\right\} \qquad (6),$$

(10) E. N. Da C. Andrade, *Nature*, **128** (1931), 835; *Phil. Mag.*, **17** (1934), 497.
(11) H. Falkenhagen and E. L. Vernon, *Phil. Mag.*, **14** (1932), 537.

in which H is the specific solutional viscosity of the solute, the viscosity of solvent being taken as unity, s the density of the solution at concentration c (g. mol/litre soln.), M_1 and M_2 the formal molecular weights of the solvent and the solute, and A the Falkenhagen−Vernon constant.

For a strong electrolyte solution (ii) where there forms a solvated or hydrated compound, formula (2) for which the Falkenhagen−Vernon effect is taken into account holds true for concentrations up to saturation:

$$\eta^{**} = 1 + \frac{(H-1)Kz_m}{1-z_m+Kz_m} + C^*(1-z_m)^{\nu_1} z_m^{\nu_2} \qquad (7)$$

where C^* is a constant independent of concentration.

The solutional viscosity of a solid in a liquid in accord with formulas (1), (6), and (7) is the viscosity probably due to the block of a secondary structure in accordance with the secondary structure theory on crystals when the substance is an organic non-electrolyte or is the viscosity due to the ionic pair when the substance is an ionic crystal.

At very dilute solutions where the solvation or hydration, though it happens, is not appreciable and the Falkenhagen−Dole−Vernon equation holds, formula (6) or (7) becomes

$$\eta^* = 1 + A\sqrt{c} + \frac{(H-1)KM_1}{1000s_1}c \qquad (8),$$

whence it readily follows that the theoretically as yet unknown factor B of the Falkenhagen−Dole−Vernon equation is defined by

$$B = \frac{(H-1)KM_1}{1000s_1}.$$

Quite recently Sulston has made careful measurements on the temperature variation of B for aqueous solutions of KCl and K_2SO_4. As we have had for KCl $H_{18}=0.9471$, $H_{25}=0.9765$, and $K=40.39$ and this K may be regarded to keep constancy for higher temperatures, we can estimate the

Table 7. The Solutional Viscosity of KCl.

t°C.	B	η_i	$\eta_{calc.}$
18	−0.0330	0.01003	0.01003
25	−0.0140	0.00874	0.00874
35	+0.0090	0.00731	0.00731
55	+0.0400	0.00540	0.00539
65	+0.0506	0.00472	0.00471
70	+0.0545	0.00442	0.00442
75	+0.0561	0.00415	0.00416
80	+0.0613	0.00392	0.00392
85	+0.0654	0.00371	0.00370

(12) W. J. Sulston, *Proc. Phys. Soc.*, **47** (1935), 657.

Table 8. I. Mixture.

Component 1	Component 2	t°C.	K	Remarks	Observer
Benzene	Toluene	25	1.23	n	Linebarger
	Diphenyl	25	0.30	n	Kendall and Monroe
	Naphthalene	25	0.49	n	,,
	Chloroform	25	(1.81)	n	Linebarger
	Carbon tetrachloride	0	1.08	n	Thorpe and Rodger
	,,	10	0.99	n	
	,,	20	0.96	n	
	,,	30	0.94	n	
	,,	40	0.88	n	
	,,	50	0.83	n	
	,,	60	0.79	n	
	,,	70	0.81	n	
	Ethylene dichloride	0	K'1.13, K''1.30	a	Faust
	,,	19.4	K'1.00, K''1.37	a	
	,,	50	K'0.72, K''1.66	a	
	Bromobenzene	18.2	1.06*	n	Yajnik and coworkers
	,,	30	1.10	n	
	,,	40	1.07	n	
	Nitrobenzene	25	0.49	n	Linebarger
	m-Nitrotoluene	15	0.40	n	Dessart
	,,	30	0.44	n	
	Methyl alcohol	25	K'0.62, K''1.60	a	Fischler
	Ethyl alcohol	25	K'1.75, K''1.45	a	Dunstan
	n-Propyl alcohol	25	K'1.70, K''2.25	a	,,
	i-Amyl alcohol	30	K'1.71, K''3.36	a	Bhide and Watson
	Phenol	20	0.087–0.23	v	Bramley
	,,	25	0.12 – 0.32	v	Swearingen
	m-Cresol	60	0.27	n	Piatti
	Guaiacol	30	0.17 – 0.29	v	Puschin and Pinter
	Ether	25	2.28	n	Linebarger
	,,	10	2.35	n	I. C. T.
	,,	20	2.20	n	
	,,	30	2.07	n	
	Anisol	0	0.83	n	Piatti
	,,	10	0.80	n	
	,,	20	0.84	n	
	,,	30	0.84	n	
	,,	40	0.89	n	

I. Mixture. (*Continued*)

Component 1	Component	t°C.	K	Remarks	Observer
Benzene	Anisol	50	0.94	n	
	,,	60	0.97	n	
	Acetone	10	1.87	n	I. C. T.
	,,	20	1.79	n	
	,,	30	1.66	n	
	,,	25	1.70	n	Fischler
	Acetophenone	16	0.65	n	I. C. T.
	Acetic acid	25	K'0.71, K''3.11	a	Dunstan
	Ethyl acetate	25	2.01	n	,,
	Ethyl benzoate	25	0.69	n	Kendall and Monroe
	Benzyl benzoate	25	0.31–0.50	v	,,
	,,	5	0.20–0.38	v	Bingham and Sarver
	,,	15	0.25–0.47	v	
	,,	25	0.31–0.53	v	
	,,	40	0.37–0.61	v	
	,,	60	0.48–0.74	v	
	m-Toluidine	15	0.18	n	Dessart
	,,	30	0.24	n	
	Pyridine	25	(0.76)	c(1:2)	Dunstan, Thole and Hunt
	Quinoline	25	0.46	n	I. C. T.
	Carbon bisulphide	25	0.91	n	Linebarger
	Sulphur chloride	15.5	0.78	n	De Carli
	,,	20	0.78	n	
	Stannic chloride	25	K'0.86, K''2.08	a	Kurnakow
	,,	70	K'0.95, K''1.68	a	

II. Mixture.

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
n-Hexane	n-Decane	25	0.74		n	Bingham, White, Thomas and Cadwell
	,,	35	0.79		n	
	,,	50	0.84		n	
	,,	65	0.87		n	
	Nitrobenzene	8	0.33 mean	1.48	n	Tab. internat., 1927–1928
	,,	15	0.33 0.33		n	
	,,	15	0.31 mean		n	I. C. T.
	,,	20	0.30 0.31	1.58 mean 1.52	n	
	,,	25	0.31		n	
	m-Nitrotoluene	15	0.28 mean	1.41	n	Dessart
	,,	30	0.29 0.29		n	
	m-Toluidine	22	0.19 mean		n	,,
	,,	32	0.20 0.20	1.60	n	
Cyclohexane	m-Nitrotoluene	15	0.36 mean	1.00 mean 0.99	n	,,
	,,	30	0.46 0.41		n	
	m-Toluidine	15	0.33 mean	0.97	n	,,
	,,	30	0.32 0.33		n	
Methyl cyclohexane	m-Nitrotoluene	15	0.30 mean	1.14 mean 1.14	n	,,
	,,	30	0.41 0.36		n	
	m-Toluidine	15	0.26 mean		n	,,
	,,	30	0.29 0.28	1.14	n	
n-Decane	n-Hexane	25	1.35	1.13	n	Bingham, White, Thomas and Cadwell
	,,	35	1.27	1.20	n	
	,,	50	1.19	1.28	n	
	,,	65	1.15	1.32	n	
Toluene	Benzene	25	0.81	1.23	n	Linebarger
	Diphenyl	25	0.24	1.25	n	Kendall and Monroe
	Naphthalene	25	0.38	1.26	n	,,
	Chlorobenzene	20	1.02 mean		n	Yajnik and coworkers
	,,	35	1.03 1.02	1.25	n	
	,,	50	1.02		n	

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Toluene	Bromobenzene	20	0.86 | mean	1.24 | mean	n	Yajnik and coworkers
	,,	35	0.85 / 0.86	1.24	n	
	m-Nitrotoluene	15	0.32 | mean	1.21	n	Dessart
	,,	30	0.36 / 0.34		n	
	Guaiacol	30	0.18–0.24	1.67–1.25	v	Puschin and Pinter
	Benzaldehyde	17	0.57	1.23	n	Schaaf
	Ethyl acetate	25	(1.63)	1.25	n	Linebarger
	Ethyl benzoate	25	0.59 | mean	1.22	n	,,
	,,	25	0.60 / 0.60		n	Kendall and Monroe
	Benzyl benzoate	25	0.25–0.39	1.92–1.23	v	,,
	m-Toluidine	15	0.15	(2.13?)	n	Dessart
	,,	30	0.21	(1.52?)	n	
Diphenyl	Benzene	25	3.33	0.30 | mean	n	Kendall and Monroe
	Toluene	25	4.10	0.30 / 0.30	n	,,
Stilbene	Dibenzyl	125	0.95		n	Beck
	Azobenzene	125	0.86		n	,,
	Benzal aniline	125	0.90		n	,,
Dibenzyl	Stilbene	125	1.05		n	,,
	Azobenzene	75	0.97		n	,,
Naphthalene	Benzene	25	2.04	0.49 | mean	n	Kendall and Monroe
	Toluene	25	2.63	0.47 / 0.48	n	,,
Tetralin	Methyl alcohol	25	(3.03)	0.21 | mean	c(1:1)	Herz and Schuftan
	Ethyl alcohol	25	(2.22)	0.22 / 0.22	c(1:1)	,,
	n-Butyl alcohol	25	K'1.72, K''1.30	0.21, 0.45	a	,,
Dekalin	*n*-Butyl alcohol	25	K'1.63, K''1.10	0.22, 0.40	a	,,

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Methylene chloride	Acetone	0	0.56	3.38	n	Sachanov and Rjachowsky
Chloroform	Benzene	25	(0.55)	1.82	n	Linebarger
	Carbon tetrachloride	25	0.52	1.79	n	,,
	Ether	0				
	,,	10	(1.13)	2.02	c(2:1)	Thorpe and Rodger
	,,	20		mean	$m = 2.62$	
	,,	30		1.87	$C_0 = 6.08\times10^3$	
	Phenetol	0	(0.56)	1.84	c(2:1)	Sachanov and Rjachowsky
	Acetone	0			c(2:1)	
	,,	20	(0.95)	1.88	$m = 2.32$	Tsakalotos
	,,	40			$C_0 = 1.52\times10^2$	
Carbon tetrachloride	Benzene	0	0.96	1.08	n	
	,,	10	1.01	0.99	n	
	,,	20	1.04	0.96	n	
	,,	30	1.06	0.94	n	Thorpe and Rodger
	,,	40	1.14	0.88	n	
	,,	50	1.21	0.83	n	
	,,	60	1.27	0.79	n	
	,,	70	1.24	0.81	n	
	Chloroform	25	1.94	0.96	n	Linebarger
	Tetrachloroethylene	25	K'1.44, K''0.94		a	Herz and Rathmann
	Tetrachloroethane	25	K'1.05, K''1.44	1.10, 1.68	a	,,
	Acetone	0	1.75	1.08	n	Sachanov and Rjachowsky
	Acetophenone	25	0.74	0.91	n	,,
Ethylene dichloride	Benzene	0	K'1.30, K''1.13	0.77, 0.89	a	
	,,	19.4	K'1.37, K''1.00	0.73, 1.00	a	Faust
	,,	50	K'1.66, K''0.72	0.60, 1.39	a	
Trichloroethylene	Pentachloroethane	25	0.41	1.71	n	Herz and Rathmann

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Tetrachloroethylene	Carbon tetrachloride	25	K'0.94, K''1.44	0.99, 1.35	a	Herz and Rathmann
Tetrachloroethane	Carbon tetrachloride	25	K'1.44, K''1.05	0.65, 1.01	a	,,
	Ether	0	2.22	1.12 } mean 1.16	n	Sachanov and Rjachowsky
	Phenetol	0	0.86	1.20 }	n	,,
	Acetone	0	1.05–1.85	1.80–1.02	v	,,
Pentachloroethane	Trichloroethylene	25	2.44		n	Herz and Rathmann
	Ether	0	1.85–3.85	1.34–0.64	v	Sachanov and Rjachowsky
	Phenetol	25	1.48	0.70	n	,,
Chlorobenzene	Toluene	20	0.98 } mean	1.27 }	n	Yajnik and coworkers
	,,	35	0.97 } 0.98	mean	n	
	,,	50	0.98	1.27	n	
	Bromobenzene	20	0.78 }	} mean 1.27	n	Unkovskaja and Volova
	,,	40	0.83 } mean		n	
	,,	60	0.83 } 0.84	1.27 }	n	Kremann, Gugle and Meingast
	,,	12	0.85 }		n	
	,,	64	0.93 }		n	
	Phenol	20	0.082–0.184	2.80–1.25	v	Bramley
Bromobenzene	Benzene	18.2	0.94 } mean	1.08 }	n	Yajnik and coworkers
	,,	30	0.91 } 0.93		n	
	,,	40	0.93 }		n	
	Toluene	20	1.16 } mean	1.06 } mean 1.07	n	,,
	,,	35	1.18 } 1.17		n	
	Chlorobenzene	20	1.28 }		n	Unkovskaja and Volova
	,,	40	1.21 } mean		n	
	,,	60	1.21 } 1.19	1.07 }	n	Kremann, Gugle and Meingast
	,,	12	1.18 }		n	
	,,	64	1.08 }		n	
	Acetone	0	1.22–1.67	1.55–1.13	v	Sachanov and Rjachowsky

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Methyl iodide	Carbon bisulphide	0	1.89	0.50	n	Thorpe and Rodger
	,,	10	1.64	0.58	n	
	,,	20	1.64	0.58	n	
	,,	30	1.45	0.66	n	
	,,	40	1.39	0.68	n	
Ethyl iodide	Methyl alcohol	20	(0.29)	2.21	n	Yajnik and coworkers
	,,	45		mean 2.20	n	
	Phenetol	0	0.47	2.19	n	Sachanov and Rjachowsky
Nitromethane	Ethyl alcohol	—	K'1.27, K''2.23	0.39, 1.09	a	Wagner
Nitrobenzene	n-Hexane	8	3.03 mean	0.50	n	Tab. internat., 1927–1928
	,,	15	3.03 3.03		n	
	,,	15	3.23 mean		n	I. C. T.
	,,	20	3.33 3.26	0.47 mean	n	
	,,	25	3.23	0.49	n	
	Benzene	25	2.04	0.49	n	Linebarger
	Methyl alcohol	25	1.32	0.49	n	Fischler
	n-Butyl alcohol	35	K'2.06, K''1.48	0.18, 0.53	a	Swearingen and Heck
	,,	45	K'1.66, K''1.61	0.22, 0.58	a	
	,,	55	K'1.53, K''1.52	0.24, 0.54	a	
	,,	65	K'1.53, K''1.47	0.24, 0.53	a	
	,,	75	K'1.50, K''1.41	0.24, 0.51	a	
	,,	80	K'1.31, K''1.60	0.27, 0.57	a	
	i-Butyl alcohol	—	K'1.02, K''3.16	0.22, 0.72	a	Wagner
	i-Amyl alcohol	0	K'1.97, K''2.25		a	Drucker and Kassel
		80	K'1.58, K''1.41		a	
	Sulphur chloride	3	1.61–2.89	0.48–0.27	v	De Carli
	,,	20	1.61–1.21	0.48–0.64	v	
	Stannic chloride	15	(1.35)		c(2:1) $m = 2.00$ $C_0 = 1.31 \times 10^2$	,,
		25	(1.70)			
	Stannic bromide	25	(1.00)		c(1:1)	,,
	,,	40	(1.00)			

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
m-Nitrotoluene	*n*-Hexane	15	3.57 mean	0.43	n	Dessart
	,,	30	3.45 3.51		n	
	Cyclohexane	15	2.78 mean	0.40	n	,,
	,,	30	2.17 2.48		n	
	Methyl cyclohexane	15	3.33 mean	0.39 mean	n	,,
	,,	30	2.44 2.89	**0.41**	n	
	Benzene	15	2.50 mean	0.42	n	,,
	,,	30	2.27 2.39		n	
	Toluene	15	3.13 mean	0.42	n	,,
	,,	30	2.78 2.96		n	
Cyanobenzene	Ethyl alcohol	—	K'0.92, K''2.00	0.53, 1.58	a	Wagner
Azobenzene	Stilbene	125	1.16		n	Beck
	Dibenzyl	75	1.03		n	,,
	Benzal aniline	75	1.03		n	,,
Water	Methyl alcohol	20				
	,,	30			c(2:1)	
	,,	40	(0.96)	0.68	$m = 2.00$	Traube
	,,	50			$C_0 = 9.2\times10^2$	
	,,	60				
	Ethyl alcohol	0				
	,,	10			c(3:1)	
	,,	20			$m = 2.00$	
	,,	30			$C_0 = 1.55\times10^3$	
	,,	40	(0.70)	0.70	&	I. C. T.
	,,	50			c(2:1)	
	,,	60			$m = 1.83$	
	,,	70			$C_0 = 4.08\times10^2$	
	n-Propyl alcohol	20			c(3:1)	
	,,	25	(0.60)	0.68	$m = 2.00$	Dunstan and Thole
	,,	30			$C_0 = 1.31\times10^3$	
	Allyl alcohol	25	(0.70)		c(4:1, 3:1, 2:1)	Dunstan
	Acetone	0	(2.97)	0.64	c(5:1)	Davis, Hughes
	,,	25	(2.58)	0.67	c(4:1)	and Jones

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Water	Formic acid	15	(0.69)	0.68 mean 0.67	c(1:1)	I. C. T.
	,,	25				
	,,	35				
	,,	45				
	,,	55				
	Acetic acid	15	(1.29)	0.67	c(1:1) $m = 1.68$ $C_0 = 1.16\times10^2$	I. C. T.
	,,	20				
	,,	25				
	,,	30				
	,,	35				
	,,	40				
	,,	45				
	,,	50				
	,,	55				
	,,	60				
	,,	65				
	,,	75				
	,,	85				
	,,	95				
	Lactic acid	25	0.28		n	Dunstan
	Formamide	25	0.48 mean	0.69	n	Merry and Turner
	,,	40	0.50 0.49		n	
	Pyridine	0	(1.19)	0.66	c(3:1+2:1)	Hartley, Thomas and Applebey
		25.08			c(3:1+1:1)	
Methyl alcohol	Benzene	25	K'1.60, K''0.62	0.63, 0.62	a	Fischler
	Tetralin	25	(0.33)	0.67	c(1:1)	Herz and Schuftan
	Ethyl iodide	20	(3.45)	0.64	n	Yajnik and coworkers
	,,	45			n	
	Nitrobenzene	25	0.76	0.64	n	Fischler
	Water	20	(1.04)	0.64 mean 0.64	c(1:2) $m = 2.00$ $C_0 = 9.2\times10^2$	Traube
	,,	30				
	,,	40				
	,,	50				
	,,	60				

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	($k\alpha$) of comp. 1 rel. to ($k\alpha$) of benzene	Remarks	Observer
Methyl alcohol	Ethyl alcohol	25	0.78	0.63	n	Bingham, White, Thomas and Cadwell
	,,	35	0.84		n	
	,,	45	0.86		n	
	,,	55	0.91		n	
	n-Propyl alcohol	25	0.63	0.65	n	Herz and Kuhn
	Ether	25	2.33–4.55	0.91–0.47	v	Baker
	Phenetol	25	1.60	0.64	n	,,
	Acetic acid	25	(1.34)	0.74	c(1:2)	Mardles
	Formamide	25	0.50 mean	0.64	n	Merry and Turner
	,,	40	0.55 0.53		n	
Ethyl alcohol	Benzene	25	K'1.45, K''1.75	0.69, 1.75	a	Dunstan
	Tetralin	25	(0.45)	0.49	c(1:1)	Herz and Schuftan
	Nitromethane	—	K'2.23, K''1.27		a	Wagner
	Cyanobenzene	—	K'2.00, K''0.92		a	,,
	Water	0	(1.43)	0.47 mean	c(1:3) $m = 2.00$ $C_0 = 1.55\times10^3$ & c(1:2) $m = 1.83$ $C_0 = 4.08\times10^2$	I. C. T.
	,,	10				
	,,	20				
	,,	30				
	,,	40				
	,,	50				
	,,	60				
	,,	70				
	Methyl alcohol	25	1.28	0.51 **0.49**	n	Bingham, White, Thomas and Cadwell
	,,	35	1.19		n	
	,,	45	1.16		n	
	,,	55	1.10		n	
	n-Propyl alcohol	25	0.88	0.47	n	Parks and Schwenck
	i-Propyl alcohol	25	0.78	0.51	n	Parks and Kelley
	Ether	25	3.30–6.60	0.65–0.32	v	Baker
	Anisol	25	K'1.81, K''1.01	0.46, 0.85	a	,,
	Phenetol	25	K'1.70, K''0.96	0.61, 0.99	a	,,
	Acetaldehyde	0	(1.7)		c(1:1, 3:1)	Leeuw
	,,	18	(1.9)			
	Acetone	25	3.7–6.9	0.47–0.25	v	Dunstan

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Ethyl alcohol	Formamide	25	0.70 } mean	0.48	n	Merry and Turner
	,,	40	0.71 } 0.71		n	
	Quinoline	25	0.89	0.51	n	I. C. T.
	Carbon bisulphide	25	2.00	0.48	n	Dunstan
	Mercaptan	25	2.70		n	,,
	Allyl thiocyanide	—	K'1.82, K''1.22		a	Wagner
n-Propyl alcohol	Benzene	25	K'2.25, K''1.70	0.44, 1.70	a	Dunstan
	Water	20	} (1.67)		c(1:3)	Dunstan and Thole
	,,	25		0.40	$m = 2.00$	
	,,	30			$C_0 = 1.31 \times 10^3$	
	Methyl alcohol	25	1.59	0.41 } mean	n	Herz and Kuhn
	Ethyl alcohol	25	1.14	0.43 } 0.41	n	Parks and Schwenck
	n-Butyl alcohol	25	0.89	0.40	n	Trew and Watkins
	Ether	25	3.88–7.75	0.55–0.27	v	Baker
	Formamide	25	K'2.30, K''0.80	0.15, 0.27	a, c(1:2)	English and Turner
i-Propyl alcohol	Ethyl alcohol	25	1.28	0.38 } mean	n	Parks and Kelley
	n-Butyl alcohol	25	0.85	0.42 } 0.40	n	Trew and Watkins
	Acetone	25	K'4.76, K''0.85	0.37, 1.47	a	Parks and Chaffee
n-Butyl alcohol	Tetralin	25	K'1.30, K''1.72	0.17, 0.38	a	Herz and Schuftan
	Dekalin	25	K'1.10, K''1.63		a	,,
	Nitrobenzene	35	K'1.48, K''2.06	0.33, 1.01	a	
	,,	45	K'1.61, K''1.66	0.30, 0.81	a	
	,,	55	K'1.52, K''1.53	0.32, 0.75	a	Swearingen and Heck
	,,	65	K'1.47, K''1.53	0.33, 0.75	a	
	,,	75	K'1.41, K''1.50	0.35, 0.74	a	
	,,	80	K'1.60, K''1.31	0.31, 0.64	a	
	n-Propyl alcohol	25	1.12	0 37 } mean	n	Trew and Watkins
	i-Propyl alcohol	25	1.17	0.35 } 0.36	n	,,
	i-Butyl alcohol	25	0.63		n	,,
	i-γ-methyl butyl alcohol	25	0.89		n	,,
i-Butyl alcohol	Nitrobenzene	—	K'3.16, K''1.02	0.16, 0.50	a	Wagner

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
i-Butyl alcohol	*n*-Butyl alcohol	25	1.59	0.23	n	Trew and Watkins
	Formamide	25	K'1.99, K''0.90	0.17, 0.44	a, c(1:2)	English and Turner
i-Amyl alcohol	Benzene	30	K'3.36, K''1.71	0.30, 1.71	a	Bhide and Watson
	Nitrobenzene	0	K'2.25, K''1.97	0.22, 0.96	a	Drucker and Kassel
	,,	80	K'1.41, K''1.58	0.35, 0.78	a	,,
	Formamide	0	K'1.77, K''1.10	0.19, 0.37	a, c(1:2)	,,
	,,	76.5	K'1.10, K''1.10	0.31, 0.37		,,
	,,	25	K'1.60, K''1.10	0.21, 0.37		English and Turner
i-γ-Methyl butyl alcohol	*n*-Butyl alcohol	25	1.25	0.29	n	Trew and Watkins
Allyl alcohol	Water	25	(1.43)	0.48	c(1:4, 1:3, 1:2)	Dunstan
Phenol	Benzene	20	4.35–11	0.23–0.09	v	Bramley
	,,	25	3.13–8.3	0.32–0.12	v	Swearingen
	Chlorobenzene	20	5.44–12	0.23–0.11	v	Bramley
	o-Cresol	25	0.69		n	Kendall and Beaver
	m-Cresol	25	0 52		n	,,
	p-Cresol	25	0.58		n	,,
	Acetone	9.95	$0.063(z_m = 0.00–0.20)$ $0.0485+0.0792z_m(z_m = 0.20–0.55)$ $-0.026+0.228z_m(z_m = 0.55–1.00)$		v	Bramley
	,,	20.05	$0.10(z_m = 0.00–0.20)$ $0.077+0.12z_m(z_m = 0.20–0.55)$ $-0.033+0.316z_m(z_m = 0.55–1.00)$		v	
	,,	29.8	$0.147(z_m = 0.00–0.20)$ $0.105+0.175z_m(z_m = 0.20–1.00)$		v	
	,,	40.1	$0.198(z_m = 0.00–0.20)$ $0.140+0.22z_m(z_m = 0.20–1.00)$		v	
	,,	49.8	$0.257(z_m = 0.00–0.20)$ $0.177+0.308z_m(z_m = 0.20–1.00)$		v	
	Dimethyl aniline	10	0.25–6.30		v	
	,,	20	0.50–4.53		v	
	,,	29.8	0.50–3.86		v	

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Phenol	Dimethyl aniline	40.2	0.60–3.10		v	Bramly
	,,	59.9	0.50–2.43		v	
	,,	80	0.50–2.10		v	
	,,	126	0.50–1.75		v	
	,,	177	1.40		n	
	Diphenyl amine	30	0.52–0.93		v	,,
	,,	40	0.55–0.95		v	
	,,	81	0.75		n	
	Diphenyl methyl amine	9.8	K'1.65, K''1.15		a	,,
	,,	20.1	K'1.44, K''1.19		a	
	,,	30	K'1.79, K''0.81		a	
	,,	40	K'1.56, K''0.92		a	
	,,	60	K'1.08, K''1.16		a	
	,,	80	K'0.91, K''1.20		a	
o-Cresol	Phenol	25	1.45		n	Kendall and Beaver
	m-Cresol	25	0.67		n	,,
	p-Cresol	25	0.68		n	,,
m-Cresol	Benzene	60	3.70	0.27	n	Piatti
	Phenol	25	1.92		n	Kendall and Beaver
	o-Cresol	25	1.49		n	,,
	p-Cresol	25	0.31–0.87		v	,,
p-Cresol	Phenol	25	1.72		n	,,
	o-Cresol	25	1.47		n	,,
	m-Cresol	25	1.16–3.23		v	,,
Guaiacol	Benzene	30	3.45–5.88	0.29–0.17	v	Puschin and Pinter
	Toluene	30	4.17–5.56	0.30–0.22	v	,,
	Acetone	30	2.00–5.56	0.85–0.31	v	,,
	Methyl aniline	30	1.41		n	,,
	Dimethyl aniline	30	2.50		n	,,

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
o-Nitrophenol	Aniline	30	K'1.10, K''1.83	0.36, 0.73	a	Bramley
	,,	40	K'0.96, K''1.76	0.44, 0.74	a	
	,,	60	K'0.91, K''1.69	0.53, 0.85	a	
	,,	80	K'0.93, K''1.55	0.59, 0.85	a	
	Pyridine	30	(1.82)	0.43	c(2:1)	,,
	,,	40	(1.54)	0.51	m = 2.00	
	,,	60	(1.35)	0.59	$C_0 = 7.02\times10$	
	,,	80	(1.19)	0.66		
Ether	Benzene	25	0.44	2.28	n	Linebarger
	,,	10	0.43	2.35	n	I. C. T.
	,,	20	0.45	2.20	n	
	,,	30	0.48	2.07	n	
	Chloroform	0	(0.89)	2.10	c(1:2)	Thorpe and Rodger
	,,	10			m = 2.62	
	,,	20			$C_0 = 6.08\times10^3$	
	,,	30				
	Tetrachloroethane	0	0.45	2.58	n	Sachanov and Rjachowsky
	Pentachloroethane	0	0.26–0.54	2.69–1.36	v	,,
	Methyl alcohol	25	0.22–0.43	2.91–1.49	v	Baker
	Ethyl alcohol	25	0.15–0.30	3.27–1.63	v	,,
	n-Propyl alcohol	25	0.13–0.26	3.15–1.58	v	,,
	Phenetol	25	0.48	2.15	n	Kendall and Wright
Anisol	Benzene	0	1.21	0.83	n	Piatti
	,,	10	1.25	0.80	n	
	,,	20	1.19	0.84	n	
	,,	30	1.19	0.84	n	
	,,	40	1.12	0.89	n	
	,,	50	1.06	0.94	n	
	,,	60	1.03	0.97	n	
	Ethyl alcohol	25	K'1.01, K''1.81	0.49, 0.89	a	Baker

II. Mixture. (*Continued*)

Component 1	Component 2	t° C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Phenetol	Chloroform	0	(1.79)	1.04	c(1:2)	Sachanov and Rjachowsky
	Tetrachloroethane	0	1.16	1.00	n	,,
	Pentachloroethane	25	0.68		n	,,
	Ethyl iodide	0	2.12	1.04 mean	n	,,
	Methyl alcohol	25	0.63	1.03 1.03	n	Baker
	Ethyl alcohol	25	K'0.96, K''1.70	0.51, 0.83	a	,,
	Ether	25	2.08	1.02	n	Kendall and Wright
	Diphenyl ether	25	0.54		n	,,
	Aniline	0	0.29		n	Bramley
	,,	10	0.32		n	
	,,	20	0.37		n	
	,,	30	0.39		n	
	,,	40	0.41		n	
	,,	60	0.47		n	
	,,	80	0.54		n	
Diphenyl ether	Phenetol	25	1.85	0.56	n	Kendall and Wright
Acetaldehyde	Ethyl alcohol	0	(0.59)	0.83	c(1:1, 1:3)	Leeuw
	,,	18	(0.53)	0.92		
Benzaldehyde	Toluene	17	1.75	0.71	n	Schaaf
	Sulphur chloride	3	0.89–0.53	0.89–1.47	v	De Carli
	,,	13.2	0.91	0.86	n	
	,,	20	1.16	0.67	n	
Acetone	Benzene	10	0.53	**1.87**	n	I. C. T.
	,,	20	0.56	**1.79**	n	
	,,	30	0.60	**1.66**	n	
	,,	25	0.59	**1.70**	n	Fischler
	Methylene chloride	0	1.79		n	Sachanov and Rjachowsky

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Acetone	Chloroform	0	(1.05)	1.78	c(1:2)	Tsakalotos
	,,	20			$m = 2.32$	
	,,	40			$C_0 = 1.52\times10^2$	
	Carbon tetrachloride	0	0.57	1.89	n	Sachanov and Rjachowsky
	Tetrachloroethane	0	0.54–0.95	2.15–1.22	v	,,
	Bromobenzene	0	0.60–0.82	1.78–1.30	v	,,
	Water	0	0.34	1.98	c(1:5)	Davis, Hughes and Jones
	,,	25	0.39	1.72	c(1:4)	,,
	Ethyl alcohol	25	0.14–0.27	3.50–1.81	v	Dunstan
	i-Propyl alcohol	25	K'0.85, K''4.76	0.47, 1.92	a	Parks and Chaffee
	Phenol	9.95	See Phenol-Acetone		v	Bramley
	,,	20.05			v	
	,,	29.8			v	
	,,	40.1			v	
	,,	49.8			v	
	Guaiacol	30	0.18–0.50	1.67–0.60	v	Puschin and Pinter
	Acetic acid	25	(0.49)	1.76	c(1:2, 1:4)	Kendall and Brakeley
	Carbon bisulphide	−13	K'1.27, K''1.16	0.75, 1.10	a	Faust
	,,	−10	K'1.02, K''1.31	0.93, 1.24	a	
	,,	0	K'1.42, K''0.89	0.67, 0.85	a	
Acetophenone	Benzene	16	1.54	0.65	n	I. C. T.
	Carbon tetrachloride	25	1.35	0.70 (mean 0.67)	n	Sachanov and Rjachowsky
	Acetic acid	25	(1.28)	0.67	c(1:1)	Kendall and Brakeley
Formic acid	Water	15	(1.45)	0.46	c(1:1)	I. C. T.
	,,	25				
	,,	35				
	,,	45				
	,,	55				

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Formic acid	Acetic acid	15	(1.87)	0.46 mean 0.47	c(1:1)	Davis and Jones
	,,	25				
	Formamide	25	(0.71)	0.48	c(1:1)	Merry and Turner
	,,	40				
Acetic acid	Benzene	25	K'3.11, K''0.71	0.32.0.71	a	Dunstan
	Water	15	(0.78)	0.86	c(1:1) $m = 1.68$ $C_0 = 1.16\times10^2$	I. C. T.
	,,	20				
	,,	25				
	,,	30				
	,,	35				
	,,	40				
	,,	45				
	,,	50				
	,,	55				
	,,	60				
	,,	65				
	,,	75				
	,,	85				
	,,	95				
	Methyl alcohol	25	(0.75)	0.87	c(2:1)	Mardles
	Acetone	25	(2.04)	0.85	c(2:1, 4:1)	Kendall and Brakeley
	Acetophenone	25	(0.78)	0.86 mean 0.86	c(1:1)	,,
	Formic acid	15	(0.53)	0.89	c(1:1)	Davis and Jones
	,,	25				
	Trichloroacetic acid	25	0.49		n	Kendall and Brakeley
	Ethyl acetate	25	2.38	0.85	n	,,
	Ethyl benzoate	25	0.89	0.82	c(1:2)	,,
	Pyridine	35	(0.93)	0.85	c(1:1) $m = 1.44$ $C_0 = 1.4\times10$ & c(5:1) $m = 2.00$ $C_0 = 3.44\times10^3$	Swearingen and Heck
	,,	45				
	,,	55				
	,,	65				
	,,	75				
	,,	80				

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Acetic acid	Stannic chloride	25.2		Polym. $\nu_1 = 3\times2, 3\times7, 3\times14$ $\nu_2 = 1\times2, 1\times7, 1\times14$		Stranathan and Strong
n-Butyric acid	Pyridine	20	(0.60)	1.32	c(3:1)	Tsakalotos
	,,	18.2	(0.60)	1.32	c(3:1)	Yajnik and coworkers
	,,	30	(0.52)	1.52	$m = 1.60$	
	,,	40	(0.40)	1.98	$C_0 = 1.60\times10^2$	
Lactic acid	Water	25	3.57	0.19	n	Dunstan
Trichloroacetic acid	Acetic acid	25	2.04	0.42	n	Kendall and Brakeley
Formamide	Water	25	2.08 mean		n	Merry and Turner
	,,	40	2.00 2.04	0.33	n	
	Methyl alcohol	25	2.00 mean		n	,,
	,,	40	1.82 1.91	0.34	n	
	Ethyl alcohol	25	1.43 mean	mean	n	,,
	,,	40	1.41 1.42	0.35 **0.34**	n	
	n-Propyl alcohol	25	K'0.80, K''2.30	0.51, 0.94	a, c(2:1)	English and Turner
	i-Butyl alcohol	25	K'0.90, K''1.90	0.26, 0.78	a, c(2:1)	,,
	i-Amyl alcohol	25	K'1.10, K''1.60	0.26, 0.46	a, c(2:1)	,,
	,,	0	K'1.10, K''1.77	0.26, 0.51	a, c(2:1)	Drucker and Kassel
	,,	76.5	K'1.10, K''1.10	0.26, 0.19		
	Formic acid	25	(1.43)	0.33	c(1:1)	Merry and Turner
	,,	40				
Ethyl formate	Stannic chloride	30		Polym. $\nu_1 = 2\times30, 2\times60, 1\times7$ $\nu_2 = 1\times30, 1\times60, 1\times7$		Kurnakow
	,,	40		Polym. $\nu_1 = 2\times30, 1\times7$		
	,,	50		$\nu_2 = 1\times30, 1\times7$		

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
i-Butyl formate	Ethyl propionate	20	1.24–0.99		v	Unkovskaja and Volova
	,,	40	1.08		n	
Amyl formate	Propyl acetate	12	1.00		n	Kremann, Gugl and Meingast
	,,	64	1.08		n	
Methyl acetate	Ethyl acetate	25	0.94	2.16	n	Chadwell
Ethyl acetate	Benzene	25	0.50	2.00 mean 2.03	n	Dunstan
	Toluene	25	(0.61)	2.03 mean 2.03	n	Linebarger
	Acetic acid	25	0.42	2.05 mean 2.03	n	Kendall and Brakeley
	Methyl acetate	25	1.06		n	Chadwell
	Benzyl benzoate	25	0.22–0.38	2.17–1.26	v	Kendall and Wright
	Aniline	0	0.13–0.19	2.31–1.58	v	I. C. T.
Propyl acetate	Amyl formate	12	1.00		n	Kremann, Gugl and Meingast
	,,	64	0 93		n	
	Ethyl propionate	20	1.47–0.96		v	Unkovskaja and Volova
	,,	40	1.02		n	
Ethyl propionate	*i*-Butyl formate	20	1.01–0.81		v	,,
	,,	40	0.93		n	
	Propyl acetate	20	0.68–1.04		v	,,
	,,	40	0.98		n	
Ethyl benzoate	Benzene	25	1.45	0.69	n	Kendall and Monroe
	Toluene	25	1.70 mean 1.69	0.73	n	Linebarger
	,,	25	1.60 mean 1.69		n	Kendall and Monroe
	Acetic acid	25	(1.12)	0.76	c(2:1)	Kendall and Brakeley
	Benzyl benzoate	25	0.50–0.59	0.96–0.81	v	Kendall and Wright
Benzyl benzoate	Benzene	25	2.00–3.23	0.50–0.31	v	Kendall and Monroe

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Benzyl benzoate	Benzene	5	2.63–5.00	0.38–0.20	v	Bingham and Sarver
	,,	15	2.13–4.00	0.47–0.25	v	
	,,	25	1.89–3.23	0.53–0.31	v	
	,,	40	1.64–2.70	0.61–0.37	v	
	,,	60	1.35–2.08	0.74–0.48	v	
	Toluene	25	2.56–4.00	0.49–0.31	v	Kendall and Monroe
	Ethyl acetate	25	2.63–4.55	0.77–0.45	v	Kendall and Wright
	Ethyl benzoate	25	1.70–2.00	0.43–0.37	v	,,
Aniline	*o*-Nitrophenol	30	K'1.83, K''1.10		a	Bramley
	,,	40	K'1.76, K''0.96		a	
	,,	60	K'1.69, K''0.91		a	
	,,	80	K'1.55, K''0.93		a	
	Phenetol	0	3.45	**0.30**	n	,,
	,,	10	3.12	**0.33**	n	
	,,	20	2.72	**0.38**	n	
	,,	30	2.54	**0.40**	n	
	,,	40	2.43		n	
	,,	60	2.11		n	
	,,	80	1.86		n	
	Ethyl acetate	0	5.23–7.69	0.39–0.26	v	I. C. T.
Methyl aniline	Guaiacol	30	0.71		n	Puschin and Pinter
Dimethyl aniline	Phenol	10	0.16–4.0		v	Bramley
	,,	20	0.22–2.0		v	
	,,	29.8	0.25–2.0		v	
	,,	40.2	0.32–1.7		v	
	,,	59.9	0.41–2.0		v	
	,,	80	0.48–2.0		v	
	,,	125	0.57–2.0		v	
	,,	177	0.71		n	
	Guaiacol	30	0.40		n	Puschin and Pinter

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Diphenyl amine	Phenol	30	1.08–1.92		v	Bramley
	,,	40	1.05–1.82		v	
	,,	81	1.33		n	
Diphenyl methyl amine	Phenol	9.8	K'1.15, K''1.65		a	,,
	,,	20.1	K'1.19, K''1.44		a	
	,,	30	K'0.81, K''1.79		a	
	,,	40	K'0.92. K''1.56		a	
	,,	60	K'1.16, K''1.08		a	
	,,	80	K'1.20, K''0.91		a	
Benzal aniline	Stilbene	125	1.11		n	Beck
	Azobenzene	75	0.97		n	,,
	Benzyl aniline	75	0.99		n	,,
Benzyl aniline	Benzal aniline	75	1.01		n	,,
m-Toluidine	*n*-Hexane	22	5.26 mean		n	Dessart
	,,	32	5.00 5.13	0.30	n	
	Cyclohexane	15	3.03 mean		n	,,
	,,	30	3.13 3.08	0.32 mean 0.31	n	
	Methyl cyclohexane	15	3.85 mean		n	,,
	,,	30	3.45 3.65	0.31	n	
	Benzene	15	5.56	(0.18?)	n	,,
	,,	30	4.17	(0.24?)	n	
	Toluene	15	6.67	(0.18?)	n	,,
	,,	30	4.76	(0.26?)	n	
Pyridine	Benzene	25	(1.32)	0.76	c(2:1)	Dunstan, Thole and Hunt
	Water	0	(0.84)	0.80	c(1:3+1:2)	Hartley, Thomas and Applebey
	,,	25.08			c(1:3+1:1)	
	o-Nitrophenol	30	(0.55)		c(1:2)	Bramley
	,,	40	(0.65)	mean	$m = 2.00$	
	,,	60	(0.74)	0.79	$C_0 = 7.02 \times 10$	

II. Mixture. (*Continued*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Pyridine	*o*-Nitrophenol	80	(0.84)	0.80	c(1:1) $m = 1.44$ $C_0 = 1.4\times10$ & c(1:5) $m = 2.00$ $C_0 = 3.44\times10^3$	Swearingen and Heck
	Acetic acid	35				
	,,	45				
	,,	55	(1.08)			
	,,	65				
	,,	75				
	,,	80				
	Butyric acid	20	(1.67)		c(1:3)	Tsakalotos
	,,	18.2	(1.67)		c(1:3)	Yajnik and coworkers
	,,	30	(1.92)		$m = 1.60$	
	,,	40	(2.50)		$C_0 = 1.6\times10^2$	
Quinoline	Benzene	25	2.17	0.46 mean	n	I. C. T.
	Ethyl alcohol	25	1.12	0.44 **0.45**	n	,,
Carbon bisulphide	Benzene	25	1.10	0.91	n	Linebarger
	Methyl iodide	0	0.53	mean **0.95**	n	Thorpe and Rodger
	,,	10	0.61		n	
	,,	20	0.61		n	
	,,	30	0.69		n	
	,,	40	0.72		n	
	Ethyl alcohol	25	0.50	0.98	n	Dunstan
	Acetone	−13	K'1.16, K''1.27		a	Faust
	,,	−10	K'1.31, K''1.02		a	
	,,	0	K'0 89, K''1.42		a	
Mercaptan	Ethyl alcohol	25	0.37	1.32	n	Dunstan
Allyl thiocyanide	Ethyl alcohol	—	K'1.22, K''1.82	0.40, 0.89	a	Wagner
Lead	Tin	400	1.15		n	Arpi
	,,	500	1.03		n	
	Bismuth	400	2.6		n	,,
	,,	500	1.6		n	

II. Mixture. (*Concluded*)

Component 1	Component 2	t°C.	K	(ka) of comp. 1 rel. to (ka) of benzene	Remarks	Observer
Tin	Lead	400	0.87		n	Arpi
	,,	500	0.97		n	
Bismuth	Lead	400	0.38		n	,,
	,,	500	0.63		n	
Sulphur chloride	Benzene	15.5	1.28	0.78 | mean	n	De Carli
	,,	20	1.28	0.78 / 0.78	n	
	Nitrobenzene	3	0.35–0.62	1.40–0.79	v	,,
	,,	20	0.83–0.62	0.59–0.79	v	
	Benzaldehyde	3	1.89–1.12		v	,,
	,,	13.2	1.10		n	
	,,	20	0.86		n	
Stannic chloride	Benzene	25	K'2.08, K''0.86	0.48, 0.86	a	Kurnakow
	,,	70	K'1.68, K''0.95	0.60, 0.95	a	
	Nitrobenzene	15	(0.74)	0.66	c(1:2)	De Carli
	,,	25	(0.59)	0.83	$m = 2.00$, $C_0 = 1.31\times10^2$	
	Acetic acid	25.2		Polym. $\nu_1 = 1\times2, 1\times7, 1\times14$; $\nu_2 = 3\times2, 3\times7, 3\times14$		Stranathan and Strong
	Ethyl formate	30		Polym. $\nu_1 = 1\times30, 1\times60, 1\times7$; $\nu_2 = 2\times30, 2\times60, 1\times7$		Kurnakow
	,,	40				
	,,	50		Polym. $\nu_1 = 1\times30, 1\times7$; $\nu_2 = 2\times30, 1\times7$		
Stannic bromide	Nitrobenzene	25	(1.00)	0.49	c(1:1)	De Carli
	,,	40				

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solutional viscosity or the viscosity of ionic pair of KCl. Column 3 in Table 7 shows thus estimated solutional viscosities, the viscosities of water at the corresponding temperatures being adopted from Internat. Crit. Tables, V.

By simple calculation, we see that these viscosity values are quite sufficiently expressed by the quadratic equation:

$$\eta_t = \frac{0.01533}{1+0.02730t+0.0001141t^2}.$$

The fact that the equation of this type has been proved by Thorpe and Rodger[13] to reproduce very closely the viscosity of numerous organic liquids without molecular complexity, and further that the magnitudes of these here obtained coefficients also are reasonably acceptable as compared with those for such liquids as ethylene chloride, carbon tetrachloride, and acid anhydrides, draws the conclusion that the solutional state of an electrolyte which is composed of its ionic pairs behave, as would be expected, like a liquid containing no molecular aggregates.

In conjunction with our study hitherto made some inquiry about the characteristic constant K along quite different lines, which we earnestly hope, may afford a clue to unvail the mysterious nature of liquids.

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Riko Majima

PROFESSOR RIKŌ MAJIMA.

On November 13th, 1934, Prof. Majima completed his sixtieth year and a feast in honour of him was given in Tokyo by his pupils, and in congratulation of this memorable day in his long life, a sum of contributions gathered among his pupils was presented to him, together with a souvenir of the occasion. On receiving it, he was good enough to give some part of it to the Chemical Society of Japan for the fund of a prize. Accordingly the Majima Prize was established, and from the year 1936 at every Annual Meeting of the Society, it shall be awarded to any person who has done an excellent work in organic chemistry or biochemistry. The papers collected in the present number of this Bulletin, all of which are the recent works of his pupils, are dedicated to Prof. Majima, and the expenses for publishing them are drawn from the same source.

Prof. Rikō Majima was born in Kyoto on the thirteenth day of November in 1874, as the eldest son of Toshitami Majima, a noted physician. His primary and middle school days were spent under his parents in this old city. Without finishing the middle school course, he came to Tokyo in order to prepare himself for the entrance examination of the First Higher School, which he passed successfully in 1890. Although in the middle school days he was rather a weak boy, he could now enjoy perfect health, for the restoration of which he tried every sports in his power: he was indeed once a member of the First Higher School Crew. It is evident that the health and the discipline given him by the sports enabled him to achieve the valuable works in later days. When he entered the Higher School he intended at first to make geology his life-work; but, advised by one of his seniors that his short-sightedness would be inconvenient for his study, he changed his course; and when he was admitted to the Tokyo Imperial University in 1896, he became a student in the Chemical Department of the Faculty of Science.

In the three years of the university life he studied inorganic chemistry under the late Prof. Edward Divers, physical chemistry and analytical chemistry under Prof. Kikunae Ikeda, and organic chemistry and part of physical chemistry under Prof. Joji Sakurai. He received also valuable instructions for the laboratory works from the late Prof. Tamemasa Haga, who had returned from Germany in 1898.

Immediately after his graduation in 1899, he was appointed Assistant and began to work under Prof. Sakurai. In 1903 he was promoted to the position of Assistant Professor. Thus Prof. Majima's research life was commenced, which, for convenience' sake, will be divided into three periods: the Tokyo period, the Sendai period, and the Osaka period.

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One of his principal research objects in his Tokyo period was *urushiol*, the main constituent of Japan-lacquer.

In January 1907 he was ordered abroad for the study of inorganic chemistry, against his own interest in the organic branch. He was obedient to the order and his scheme was first to visit Prof. A. Werner, the brilliant initiator of the Co-ordination Theory. When he arrived in Europe, however, a telegram from the Japanese Government commanded him to take organic chemistry as his subject. This unexpected but agreeable change drove him immediately for Kiel from Zürich. It was quite natural that he should have done so, because at the Kiel University there was Prof. Harries, inventor of ozonolysis, probably the best method for the exploration of the constitution of *urushiol*.

At Kiel he was working hard upon *terpene* and partly upon *urushiol*. But unfortunately in the following year he suffered from influenza which brought pneumonia. Soon after recovery he was again infected with erysipelas which was followed by nephritis. Thus he was forced twice to lie in bed in the Kiel University Hospital. Then he had to stay at the noted spa Wildungen to ensure complete recovery. It was only after one complete summer semester had passed that he could return to the laboratory. His research work there was kept on again from the beginning of the winter semester of the year 1908 until the end of the summer in 1909.

From the winter semester of the year 1909 until the end of the summer in 1910, he stayed at Zürich under Prof. R. Willstätter, with whom he worked on some oxidation mechanism of aniline.

Then he went over to England to inspect the state of things in the study of chemistry and spent some time at the Davy-Faraday Research Laboratory of the Royal Institution in London. Then passing through the United States of America, he returned to Japan on March 3rd in the year 1911.

Just at that time the Faculty of Science of the Tōhoku Imperial University was newly founded at Sendai. ("Tōhoku" means north-east. This university is so called as Sendai is situated in the north-eastern part of Japan proper). The Faculty was ready to receive him in 1911 as one of the professors. Prof. Majima's Sendai period was thus begun and it was in this period that the works upon *urushiol* were published. For this research, in 1913 he was honoured with the Sakurai Prize from the Tokyo Chemical Society and then in 1917 with the Imperial Academy Prize from the Imperial Academy of Japan.

His research field, however, was not confined only to *urushiol*; he also found a new synthetical method for obtaining *indole* by a pyrogenetic reaction of *aniline* and *acetylene*. His endeavour was then naturally directed to the synthetical works upon various *indole* derivatives.

His interest was also directed to many natural colouring matters, e.g. *shikonin*, *carthamin*, and many other sorts of *anthocyanins* (studied partly with Miss C. Kuroda), *mangostin* and *fukugetin* (studied by M. Murakami); and also to synthetical pigments, e.g. some new classes of vat dyes (by M. Nakanishi) and various sorts of photographic sensitizers (by T. Ogata and S. Sakurai). They should specially be cited, as those studies were all executed in Prof. Majima's laboratory under his zealous encouragement.

In his endeavour to elucidate the constitution of *aconitine*, Prof. Majima showed a fair example of his character, or the spirit fighting against a difficult problem to explore the mystery wrapped in it.

Aconitine, the alkaloid of aconitum roots, has many hydroxyl-groups and, indeed, an unparallelled complex nature. Prof. Majima began the study in collaboration with T. Suginome, S. Morio, and H. Shimanuki, and is still continuing it step by step assisted by K. Tamura. Assuredly the difficulties of isolating the *aconitine* in pure state greatly puzzled him in his earlier experiments, but his strenuous efforts brought him a clear decisive result. He could isolate the four sorts of *aconitines*, i.e. *aconitine*, *mesaconitine*, *hypaconitine*, and *jesaconitine*, in pure forms, from about sixteen different species of aconitum plants.

In 1926 he was elected Member of the Imperial Academy of Japan, and although he was rather a man in the laboratory, he was compelled gradually to take up many administrative responsibilities with relation to the universities in Japan. He became, in 1926, the Director of the Faculty of Science of the Tōhoku Imperial University, which post he held until 1928. He was appointed, in 1927, head of the Organizing Committee of the Science Faculty of the Hokkaido Imperial University which was to be established at Sapporo, and he was, in 1930, appointed Director of that newly opened Faculty, in which post, however, he remained only for a year, as an additional one to the professorship at Sendai. Meanwhile he was also a member of the Organizing Committee of the Department of the Dyestuff-Chemistry of the Tokyo University of Engineering.

In 1931 he was again a member of the Organizing Committee, this time, of the Faculty of Science of the Osaka Imperial University, and was appointed Professor and Director of this new faculty since its foundation in 1932. In 1933, he and his family left Sendai, where they had lived twenty-two long years, and removed to Osaka. Thus his Osaka period was begun.

It is the present writer's happy duty to report that he is still assiduously engaged in his research works on *aconitines*, etc., in his new laboratory, with the same health and energy as were enjoyed in his Sendai period. He

may perhaps thus be making good for the time long lost in the administrative affairs in the various universities.

Outside the universities he has been also active since 1917 as a member of the research staff of the Institute of Physical and Chemical Research, Tokyo; since 1920 as a member of the National Research Council of Japan ("Gakujutu Kenkyu Kaigi"); and since 1933 as a member of a committee of the Foundation for the Promotion of Scientific and Industrial Research of Japan ("Nippon Gakujutu Sinko Kai"). In 1924 Prof. Majima was sent to the Fifth Conference of the International Union of Pure and Applied Chemistry held at Copenhagen as the delegate of the National Research Council of Japan. In 1927 he was elected Honorary Member of the Chemical Society of Holland.

Prof. Majima's life is not complete if his literary work is left unmentioned. It is the compilation of the complete abstracts of Japanese chemical literatures. For this painstaking work he received donations from the "Keimei Kai" Foundation and was also given contributions from many supporters. Consequently he was able to found a society called "Nippon Kagaku Kenkyu Kai" in 1926, with the sole purpose of continuing the work already commenced as early as 1918 and of publishing the materials thus accumulated. In the year 1927 the first product of his endeavours appeared in the form of a book entitled "Nippon Kagaku Sōran" Vol. I, which covers the period of 1877–1900. Since then Vol. II (1901–1908), Vol. III (1909–1913), Vol. IV (1914–1017) and Vol. V (1918–1921) have all been published. Besides these a monthly magazine with the same title has also been edited by him. It publishes the complete abstracts of the current Japanese chemical literatures, beginning with the year 1927. The gap between the year 1922 and 1926 will be filled with two more volumes of the "Nippon Kagaku Sōran" which are now ready in press. Needless to say, these publications were received with enthusiasm by the Japanese chemists as well as by the whole circles of the scientists in the country.

The green old age of Prof. Majima, who has played such an important rôle in promoting the scientific education and research in Japan and especially served in elevating his special domain of organic chemistry in this country up to the present state, should heartily be congratulated not only by his pupils but by all the Japanese chemists, wishing on their part for his further aid for the future advancement of chemistry in Japan.

Sin'iti KAWAI.

February, 1936.

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ON THE COMPOSITION OF RAPE SEED OIL.

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Numerous studies on the rape seed oil have hitherto been published, and the composition of the fatty acid mixture from the oil has been considered generally as follows:[1] myristic acid 1.5%, stearic acid 1.5%, arachidic acid 1.5%, oleic acid 19.5%, erucic acid 60%, linolic acid 14%, and linolenic acid 2% (total 100%). This composition corresponds to an oil with the saponification value 171 and the iodine value 88.7. But rape seed oil, as well known, has generally saponification value 172–175 and iodine value 99–103, and such a low iodine value as the above-mentioned (88.7, nondrying oil) has never been found in any of the rape seed oils prepared from the various sorts of the seed.[2] The authors describe in this paper the quantitative determination of the composition of rape seed oil.

The sample oil employed in this study had moderate numbers for rape seed oil: $d_4^{15.5°}$ 0.9147, viscosity (Redwood) at 104°F. 186 sec., at 210°F. 55 sec., flash point 278°C., cloud point −14°C., pour point −17°C., acid value 1.3, saponification value 174, iodine value (Wijs) 101, moisture 0.2%, and hexabromide value 7.66 (corresponding to 2.81% of linolenic acid by calculation).

Rape seed oil (1 kg.) was saponified with 4 N alcoholic potash, the solvent was evaporated, the residual soap was dissolved in water, and the solution

Fraction	Temperature °C./10 mm.	Yield (g.)	Saponif. value	Iodine value	Saponif. value calculated as methyl ester (F_1)
I	−200	50	200	94.6	C_{17} acid 199
II	200–210	400	189	132	C_{18} ,, 189
III	210–215	25	183	86.4	C_{19} ,, 181
IV	215–220	40	175	—	C_{20} ,, 173
V	220–230	250	163	74.5	C_{21} ,, 166
VI	230–235	100	160	73.3	C_{22} ,, 159
VII	residue	85	—	—	—
	loss	50			

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(2) Lewkowitch, "Chem. Tech. and Analy. of Oils, Fats and Waxes", Vol. II (1914), 262. Ubbelohde, "Chem. Analy. und Technol. d. Öle u. Fette", Vol. II (1920), 176. Grün, *ibid.*

was acidified and extracted with ether. The ethereal solution was concentrated, and the resulting fatty acid was converted into the methyl ester, which was then subjected to fractional distillation under diminished pressure. After 9 rectifications, fractions I–VII were obtained.

Fraction I was further fractionated:

Fraction	Temperature °C./25 mm.	Yield (g.)	Saponif. value	Iodine value	Saponif. value calculated as methyl ester (F_1)
1	135–195	5	213	—	C_{15} acid 221
2	195–210	10	210	77.6	C_{16} ,, 209
3	210–220	10	201	86.7	C_{17} ,, 199
4	220–228	10	201	96.0	,, ,, ,,
5	228–248	5	—	—	
6	residue	10	—	—	

From fraction 1 fatty acid mixture was liberated and separated by means of lead salt alcohol method into two following portions:

solid acid, yield 2.4 g., neutralization value 215, m.p. 57°C.; liquid acid, yield 2.0 g., neutralization value 202, iodine value 104.

By recrystallization of the solid acid, palmitic acid was isolated and it was confirmed by mixed-melting method. The liquid acid seemed to be a mixture of oleic, linolic and a small amount of palmitic acids. The existence of myristic acid and palmitoleic acid was doubtful.

Fraction II (30 g.) was subjected to lead salt ethanol method:

solid acid, yield 3 g.; liquid acid, yield 25 g., neutralization value 190, iodine value 144.

The above solid acid was fractionally recrystallized:

Fraction	Yield (g.)	M.p. (°C.)	Neutralization value	Iodine value
1	0.7	60.5–61	204	—
2	1.2	52.5–55	194	—
3	0.9	51–55	179	51.3

Fraction 1 was confirmed to be palmitic acid by mixing with pure acid, and fraction 3 was considered to be crude erucic acid from its neutralization and iodine values. Contrary to our anticipation, stearic acid could not be obtained; if stearic acid were present, it would crystallize out first in the 1st

crystalline fraction before palmitic acid. Fraction 2 seemed to be a mixture of erucic acid and palmitic acid.

The liquid acid portion of fraction II was a mixture of oleic, linolic, and a minute quantity of linolenic acids, judging from the neutralization and iodine values and the yield of its hexabromide.

As the existence of oleic and linolic acids in rape seed oil was already confirmed by Toyama,[3] isolation and identification of these acids were omitted in this study.

From fraction III liquid C_{18}-acid and solid C_{22}-acid were obtained.

Fraction IV (40 g.) was separated into two following portions by the usual method.

Solid acid, yield 16 g., neutralization value 173; liquid acid, yield 21 g., neutralization value 191, iodine value 92.7.

The solid acid was recrystallized:

Fraction	Yield (g.)	M.p.(°C.)	Neutralization value	Iodine value
1	2	33-34	167	66.6
2	3	33-34	170	73.7
3	10	—	175	—

Namely, only erucic acid was isolated and no arachidic acid seemed to exist in this oil.

Fraction V and VI were obviously methyl erucate.

Fraction VII (residue) (85 g.) was saponified and the unsaponifiable matter was extracted with ether. From the aqueous layer, mixed acids were liberated and recrystallized from methanol.

Crystal	Yield (g.)	M.p.(°C.)	Neutralization value	Iodine value
1	1	76.5-77.5	167	0.5
2	2	33-35	166	74.7
3	21.5	32-33.5	169	74.1
4	25	32-33.5	168	76.2
5	16.5	32.5-33.5	167	75.5
6	10	32-33.5	166	73.7
7	5	28-29	165	73.7

(3) *J. Soc. Chem. Ind., Japan*, **25** (1922), 1044; *Chem. Umschau, Fette, Öle, Wachse, Harze*, **30** (1923), 88.

Crystals 1 and 4 were identified with pure behenic and erucic acids respectively by the usual mixing test. On the other hand, the ethereal layer was concentrated and about 7 g. of brassicasterine[4] was obtained.

Summary.

The composition of rape seed oil was determined and the contents of the fatty acids were calculated from the chemical numbers of the original oil and each fraction: behenic acid 0.8%, erucic acid 55%, oleic acid 14%, linolic acid 24%, linolenic acid 2%, and palmitic acid 3.5%. Myristic, palmitoleic, and stearic acids, however, could not be found.

The Osaka Municipal Institute of Industrial Research.

ÜBER DIE PRODUKTE DER EINWIRKUNG VON MONOCHLORESSIGSÄURE AUF NAPHTHOLE.

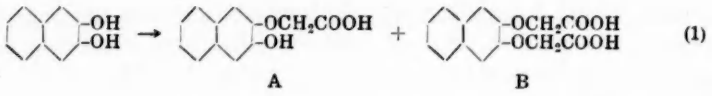
Von **Rin-nosuke SHIBATA** und **Minoru OKUYAMA.**

Eingegangen am 15. Oktober 1935. Ausgegeben am 28. März 1936.

Einleitung. Beim Erhitzen äquimolekularer Mengen von Monochloressigsäure mit β-Naphthol in Gegenwart von Kalilauge wird β-Naphthoxyessigsäure[1] kondensiert. In analoger Weise wirkt Monochloressigsäure auf Dioxynaphthalin. So hat man aus 2,3-Dioxynaphthalin 2-Naphthol-3-oxyessigsäure (Formel A) vom Schmp. 153°, in farblosen Nadeln aus Wasser gewonnen, die gegenüber 2,3-Dioxynaphthalin wesentlich gesteigerte Baumwollaffinität zeigt und bei der Faser mit diazotiertem *p*-Nitranilin einen durch Schönheit ihrer Tönung hervorragenden, roten Farbstoff ergibt, der freilich in der Echtheit hinter der Naphthol-AS-Färbung zurücksteht. Dabei hat man noch eine Spur von 2,3-Naphthalindioxyessigsäure (Formel B) erhalten, aber aus 2,7-Dioxynaphthalin, nur Mono-oxyessigsäure vom Schmp. 202–203°.

(4) Siegfeld, *Z. Nahr. Genussm.*, **17** (1904), 581. Windaus and Welsch, *Ber.*, **42** (1909), 612. Marcusson and Meyerheim, *Z. angew. Chem.*, **27** (1914), 201. Schmid and Waschkau, *Monatsh.*, **48** (1927), 139.

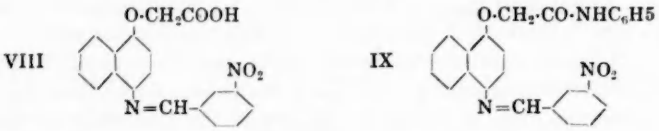
(1) F. Spitzer, *Ber.*, **34** (1901), 3191.



Verfasser hat früher bei Herrn Prof. Hans Bucherer diese Reaktion[2] untersucht. Es handelte sich damals jedoch anfänglich darum, eine Hydroxylgruppe von Dioxynaphthalin zu besetzen, um die Reaktion mit *p*-Dimethylamino-anilin-*o*-thiosulfonsäure zu vereinfachen.

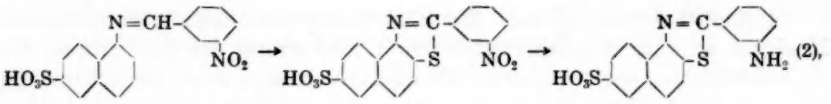
In vorliegender Arbeit wollte Verfasser weiter möglichst viele Produkte dieser Reihe synthetisieren, um den Einfluss der Oxyessigsäuregruppe des Naphthalinkerns auf die Naphthole sowie ihre Abkömmlinge in ihrer Substantivität näher unterzusuchen, wie er sich beim 2,3-Dioxynaphthalin so ausgezeichnet hatte erweisen lassen.

***α*-Naphthol.** Zunächst haben wir aus *α*-Naphthol folgende Verbindungen synthetisiert: I. 1-Naphthoxyessigsäure, Schmp. 193.5°, farblose Nadeln aus Benzol; II. 4-Nitronaphthyl-1-oxyessigsäure, Schmp. 217°, gelbe Nadeln aus Xylol; III. 4-Aminonaphthyl-1-oxyessigsäure-chlorhydrat, Schmp 231°, farblose Nadeln aus Äthanol, dessen freie Base: IV. Schmp. 220–225° (zers.) und farblose Nadeln zeigte; V. 4-Nitronaphthyl-1-oxyessigsäureanilid, Schmp. 181.5°, schwach gelbe Nadeln aus Alkohol; VI. 4-Nitronaphthyl-1-oxyessigsäure-1′-Naphthyl-amid, Schmp. 241°, farblose Nadeln aus Aceton; VII. 4-Aminonaphthyl-1-oxyessigsäureanilid, Schmp. 142.5°, farblose Nadeln aus Ligroin-Benzol; VIII. *m*-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäure, Schmp. 182.5°, gelbe, lange Blättchen aus Alkohol; IX. *m*-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäureanilid, Schmp. 217.5°, gelbe Nadeln aus Aceton und X. *p*-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäure, Schmp. 243°, gelborange farbige Nadeln aus Aceton.

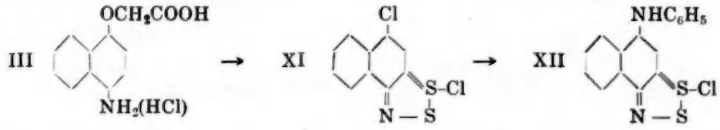


Durch die Synthese der Verbindungen II mit X wollten wir ein neues, eine Oxyessigsäuregruppe enthaltendes Thiazol gewinnen, nach dem Verfahren des D. R. P. 165 226 über Benzylidenverbindung, mit Hilfe von Schwefel und Schwefelnatrium (Gleichung 2):

(2) Näheres darüber wird vielleicht später von Herrn Prof. Bucherer veröffentlicht werden.



aber hatten gar keinen Erfolg damit. Zum selben Zweck haben wir die Verbindung III mit Schwefelchlorür nach Herz[3] behandelt und dadurch eine gelbbraune Substanz erhalten, die mit Anilin eine in goldglänzende, tief violette Blättchen auskrystallisierende Verbindung bildet. Sie hat nach der Analyse die Zusammensetzung $C_{16}H_{11}S_2N_2Cl$ und stimmt in allen Eigenschaften mit dem Anilid überein, welches Vannotti[4] nach Herz über Thiazthioniumchlorid des 1-Naphthylamins synthetisiert hat. Danach wirkt Schwefelchlorür auf die Verbindung III auf zwei Weisen: einerseits durch einen Ringverschluss zusammen mit der Aminogruppe zum Thiazthioniumchlorid, anderseits zugleich mit einer Kernsubstitution des Chloratoms durch Verdrängen der Oxyessigsäuregruppe:



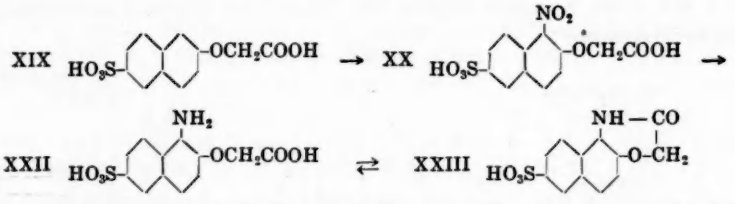
Dieses Anilid färbt Wolle und tanningebeizte Baumwolle bordeauxrot, ganz wie ein basischer Farbstoff.

β-Naphthol. Durch Nitrierung der β-Naphthoxyessigsäure erhält man zwei Nitrokörper. Der eine, 1-Nitroverbindung XIII, gelbe Nadeln aus Eisessig vom Schmp. 191–192°, bildet das Hauptprodukt, dessen Anilid XV bei 169° schmilzt und aus Alkohol gelbe Mikrokrystalle darstellt. Der andere XIV, der daneben entsteht schafft auch gelbe Nadeln aus Eisessig, welche zwischen 157 und 185° schmilzt, liefert jedoch ein ganz anderes Anilid XVI, welches aus Äthanol schwach gelbe, lange, etwas biegsame Nadeln vom Schmp. 217° darstellt. Durch Reduktion gibt der erste sowie sein Anilid ein und dasselbe Produkt XVII vom Schmp. 218–219°, welches aus Alkohol farblose Nadeln darstellt und nichts anderes als das innere Anhydrid der 1-Aminonaphthyl-2-oxyessigsäure ist, der zweite dagegen eine braungelbe Substanz XVIII vom Schmp. 187–188°, vielleicht 6-Aminonaphthyl-2-oxyessigsäure, welche aus Alkohol in Nadeln krystallisiert.

(3) Richard Herz, D.R.P. 360690 (Frdl. XIV. 908).
(4) F. Vannotti, Dissertation der Eidg. Techn. Hochschule, Zürich (1933).

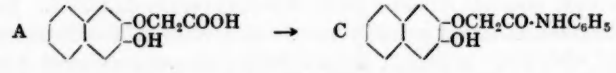
2-Naphthol-6-sulfosäure. Zunächst wendet man Schäffersche Säure als Naphthol an, um möglicherweise durch Einführung der Sulfogruppe die Anhydridbildung der 1-Aminonaphthyl-2-oxyessigsäure zu verhindern und um ferner damit auch ein Thiazol über die entsprechende Benzylidenverbindung zu synthetisieren.

2-Naphthoxyessig-6-sulfosäure XIX bildet ein Dinatriumsalz, welches aus Wasser mit 2 Mol. Krystallwasser farblose Blättchen darstellt, wohingegen man aus der verd. Salzsäure Mononatriumsalz ohne Krystallwasser erhält. Durch Nitrierung gewann man 1-Nitrokörper XX, das Hauptprodukt und konnte aus dessen Mutterlauge ausserdem etwas 4-Nitrokörper XXI, ein Nebenprodukt in braungelben Nadeln, isolieren. Durch Reduktion gab 1-Nitrokörper XX wieder inneres Anhydrid XXIII, welches man jedoch durch Kochen mit Natronlauge in freie Oxyessigsäure XXII verwandeln kann:



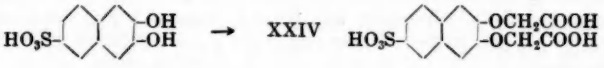
Aber es ist uns noch nicht gelungen, daraus ein Thiazol zu synthetisieren. 1-Aminonaphthyl-2-oxyessig-6-sulfosäure XXII ist diazotierbar und kuppelt sich mit β-Naphthol zu einem blaustichigen, roten, sauren Farbstoff.

2,3-Dioxynaphthalin-6-sulfosäure. Zur Erlangung der Substantivität der 2-Naphthol-3-oxyessigsäure sollte man sie weniger wasserlöslich machen. Es wäre also zweckmässiger, die Säure in ihr Anilid (Formel C) zu verwandeln:

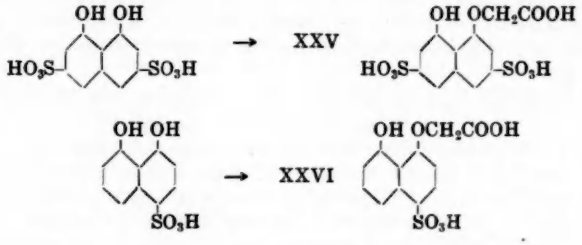


Im Gegensatz zu diesem allgemeinen Gedanken hat man zunächst 2,3-Dioxynaphthalin-6-sulfosäure angenommen. Statt, wie aus 2,3-Dioxynaphthalin und Monochloressigsäure, bei Gegenwart von Soda hauptsächlich Monooxyessigsäure und nur spurweise Dioxyessigsäure zu bekommen, verläuft die Reaktion mit 2,3-Dioxynaphthalin-6-sulfosäure gerade umgekehrt. Das heisst, die entsprechende Dioxyessigsäure XXIV ist das einzige Produkt. Man konnte dies nicht verhindern, weder durch Anwendung von weniger Soda, noch durch sonstigen milderen Kondensationsverfahren, z.B. Natriumacetat statt Soda und niedrigerer Temperatur. Dioxyessigsäure XXIV hat Kupplungsfähigkeit, obwohl die so gewonnenen Azofarbstoffe wegen ihres unschein-

baren, hellorangen Farbtons technisch wertlos sind. Beide sind vielleicht die Folge des Vorhandenseins der Sulfogruppe in 6-Stellung.



1,8-Dioxynaphthalin-sulfosäure. Nächst der 2,3-ortho-Stellung hat man die 1,8-peri-Abkömmlinge untersucht. Als Einwirkungsprodukt der Monochloressigsäure auf die Chromotropsäure in Gegenwart von Soda entsteht allein die entsprechende Mono-oxyessigsäure XXV, deren Mononatriumsalz in farblosen Nadeln aus Wasser krystallisiert.



Sie kuppelt sich mit dem diazotierten *p*-Nitranilin zu einem roten Azofarbstoff, der als Säurefarbstoff Wolle in einem klaren, leuchtend roten Farbton färbt.

Auf dieselbe Weise gewinnt man aus Dioxynaphthalin-sulfosäure S auch nur eine Monooxyessigsäure XXVI, die aus Wasser in farblosen Nadeln krystallisiert und sich mit dem diazotierten *p*-Nitranilin zu einem roten Azofarbstoffe kuppelt, der als Wollfarbstoff dient.

In beiden Fällen wurde durch Einführung einer Oxyessiggruppe der Farbton der Farbstoffe mit der Veränderung des ursprünglich blaustichigen Rots in klares, reines Rot beeinflusst. Das Verhalten der Farbstoffe gegen die Metallbeize wurde so beeinflusst, dass die Farbveränderung durch Nachbehandlung augenscheinlich schwächer wurde.

Diese Untersuchung ist noch im Gang, aber vorliegende Mitteilung möchten wir doch hier bringen, als einen kleinen Beitrag zur Festschrift für unseren hochverehrten Professor Dr. Rikō Majima, und dabei ihm auch hier unsre besten Glückwünsche aussprechen.

An dieser Stelle sagen wir auch der Japanische Gesellschaft zur Förderung der Wissenschaft und Industrie für ihre grosszügige Unterstützung unseren verbindlichsten Dank.

Beschreibung der Versuche.

I. α-Naphthol. (1) *α-Naphthoxyessigsäure.*[1][5] 20 g. α-Naphthol wurde in 72 g. Kalilauge (1 : 2) gelöst. Nach Verdünnen mit 200 c.c. Wasser wurde die Lösung bei 100° unter Umrühren erhitzt, wobei man innerhalb von etwa 2 Stunden eine Lösung von 19 g. Monochloressigsäure in 90 c.c. Wasser langsam zufliessen lässt. Nach vollständigem Eingetropfeln der Lösung wurde alles noch eine halbe Stunde lang erwärmt. Den Reaktionsendpunkt erkennt man, wenn die Kupplungsfähigkeit verschwindet. Nach beendeter Reaktion wurde das Gemisch abgekühlt und mit verd. Salzsäure deutlich sauer auf Lackmuspapier angesäuert, woraufhin Oxyessigsäure ausschied. Man saugt die Niederschläge ab, wäscht mit kochendem Wasser, trocknet und löst alles in 80 c.c. Alkohol. Nach dem Entfärben mit Tierkohle lässt man die Lösung in 160 c.c. Wasser einfliessen, worauf die Säure in farblosen Säulchen auskrystallisiert. Nach dem Umkrystallisieren aus Benzol zeigte das reine Präparat den Schmp. 193.5°. Die Ausbeute betrug 20–25 g. α-Naphthoxyessigsäure ist leicht löslich in Äthanol, Methanol, Äther, Aceton, Essigester sowie Toluol und ein wenig löslich in Benzol sowie Schwefelkohlenstoff. Sie hat keine Kupplungsfähigkeit.

(2) *4-Nitronaphthyl-1-oxyessigsäure.*[1][5] 17 g. α-Naphthoxyessigsäure in 60 c.c. Eisessig wurden bei 20–30° mit 26 c.c. Salpetersäure von 40° Bé nitriert. Man saugt die so gewonnene gelbe Paste ab und wäscht sie mit Eisessig, danach mit Wasser aus, trocknet und krystallisiert sie aus Eisessig um. Schöne gelbe Säulchen vom Schmp. 215°–216°. Die Ausbeute betrug 15 g. Nach dem Umkrystallisieren aus Xylol Schmp. 217°. Sie ist leicht löslich in Äthanol, Methanol, Aceton, Eisessig sowie Essigester und ein wenig in Äther, Benzol, Toluol, Xylol sowie in Wasser.

(3) *4-Aminonaphthyl-1-oxyessigsäure.*[1] 5 g. feinpulveriger Nitrokörper in 40 c.c. Eisessig wurden bei 100–110° mit 8 g. Zinnpulver und 20 c.c. konz. Salzsäure reduziert, nach Beendigung der Reaktion mit 400 c.c. heissem Wasser verdünnt und heissfiltriert. Man entfernt das in die Lösung übergegangene Zinn mittels Schwefelwasserstoff und engt das Filtrat unter vermindertem Druck ein, wodurch man Chlorhydrat des Aminokörpers in farblosen Nadeln vom Schmp. 230° (zers.) gewinnt. Die Ausbeute betrug 4.1 g. Die freie Base kann man aus der alkalischen wässerigen Lösung durch Ansäuern mittels Essigsäure isolieren. Nach Umkrystallisieren aus Äthanol zeigt die reine, freie Base den Schmp. 220–225° (zers.) und stellt farblose Nadeln dar.

Behandelt man die Salzsäurelösung des Aminokörpers mit Natriumnitrit, so tritt eine blaue Farbe[6] auf. Der diazotierte Aminokörper kuppelt sich mit β-Naphthol zu einem violettroten Azofarbstoff.

Der Aminokörper ist in verd. Alkalien leicht löslich, aber kaum in verd. Mineralsäure und ein wenig löslich in heissem Wasser, in organischen Lösungsmitteln aber meistens nicht löslich, jedoch in Essigester wieder ziemlich leicht löslich. Für Analyse wurde die Substanz über Benzylidenverbindung (Formel VIII) gereinigt. (Gef.: N, 5,55. Ber. für $C_{12}H_{12}NO_3Cl$: N, 5.53%.)

(4) *m-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäure.* Durch 2 stündiges Kochen von 5 g. Aminokörper in 20 c.c. verd. Natronlauge und 20 c.c. Wasser mit 4 g. *m*-Nitro-

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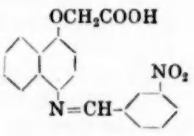
(5) B.H. Ingham, *J. Chem. Soc.*, **1931**, 895.

(6) Jacobs und Heiderbergér, *J. Am. Chem. Soc.*, **39** (1917), 2217, erklärten diese Erscheinung als einer partiellen Oxydation.

VIII 

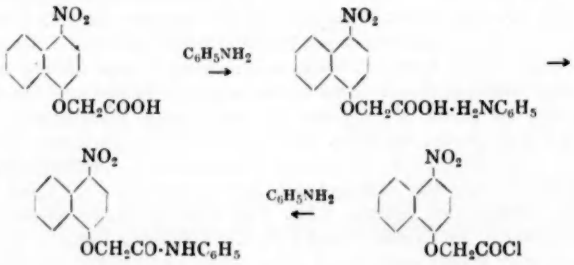
benzaldehyd scheidet die Benzylidenverbindung in gelben Blättchen aus. Zieht man den Krystallbrei aus und erwärmt ihn mit verd. Essigsäure, so erhält man die Säure im freien Zustand. Rohausbeute 4.5 g. Nach Umkrystallisieren aus Alkohol zeigt sie den Schmp. 182.5°. Durch Kochen mit verd. Mineralsäure spaltet sie sich leicht in den Aminokörper und in Aldehyd. Sie ist leicht löslich in Äthanol, Methanol, Äther, Aceton, Toluol sowie Essigester und ein wenig in Benzol. (Gef.: N, 7.65. Ber. für $C_{19}H_{16}N_2O_6$: N, 7.63%.)

(5) *1-Nitronaphthyl-4-oxyessigsäureanilid.* 1-Nitronaphthyl-4-oxyessigsäure wirkt durch gelindes Erwärmen leicht auf Anilin, wodurch sich eine lockere Verbindung bildet, vielleicht von der Zusammensetzung $C_{18}H_{16}N_2O_5 \cdot C_6H_5NH_2$, die so unbeständig ist, dass sie sich durch Kochen in organischen Lösungsmitteln schon abgespaltet. Nach sorgfältigem Umkrystallisieren aus Alkohol erhielt man aus ihr schwachgelbe, feine Nädelchen, welche bei 124–125° fast völlig schmelzen, aber gänzlich erst bei 218°.

Durch 10-stündiges Kochen einer Lösung von 2.5 g. Nitrokörper in 10 g. Anilin erhält man aber 2.5 g. Anilid vom Schmp. 181.5° in schwachgelben Nadeln, was ganz mit dem Anilid, das man über dem Säurechlorid synthetisiert hat, übereinstimmt (Mischschmelzpunkt). (Gef.: N, 9.02. Ber. für $C_{18}H_{14}N_2O_4$: N, 8.70%.)

In eine Suspension von 7.5 g. gut getrockneter Nitrokörper in 80 c.c. Benzol wurden 6 g. Phosphorpentachlorid in 60 c.c. Benzol unter Umrühren langsam getropfelt. Nach 2-stündigem Erhitzen engt man die Benzollösung auf etwa ein Drittel des Volums ein, fügt dasselbe Volum Petroläther hinzu, und lässt alles so stehen, worauf das Säurechlorid in schwachgelben Nadeln ausscheidet. Nachdem Umkrystallisieren aus Benzol-Ligroin wurden 7.8 g. vom Schmp. 96° erhalten.

Durch Eintun von 2.5 g. Säurechlorid in 2.5 g. Anilin tritt sofort die Reaktion ein, wobei sich Gas und Wärme entwickeln. Man lässt sich alles durch Erhitzen lösen, fügt die dreifache Menge Alkohol hinzu, worauf das Anilid in schwachgelben Nadeln ausscheidet. Nach Umkrystallisieren aus Alkohol wurden 3.3 g. vom Schmp. 181.5° erhalten. Die Reaktion verläuft also folgendermassen:



Das Anilid ist in Aceton, Nitrobenzol sowie Anilin leicht löslich und beim Kochen ziemlich leicht löslich in Alkohol, Benzol sowie Methanol. Man kann das Anilid in Mineralsäure erwärmen, ohne dass es sich zersetzt.

(6) *1-Nitronaphthyl-4-oxyessigsäure-1'-naphthylamid.* Aus 2 g. α-Naphthylamin in 10 c.c. Alkohol und 2.5 g. Säurechlorid wurde 2.5 g. Naphthylamid gewonnen. Nach

Umkrystallisieren aus Aceton fast farblose Nadeln vom Schmp. 241°, welche in Wasser, verd. Säure u. Alkalien beständig sind. Es ist in den meisten organischen Lösungsmitteln wenig löslich. (Gef.: N, 7.67. Ber. für $C_{22}H_{16}N_2O_4$: N, 7.52%.)

(7) *1-Aminonaphthyl-4-oxyessigsäureanilid.* 1.4 g. 1-Nitronaphthyl-4-oxyessigsäureanilid in 90 c.c. Alkohol wurde mit 2 g. Zinnpulver und 7 c.c. konz. Salzsäure reduziert. Nach weiterem 30 Minuten langen Erhitzen filtriert man heiss und kühlt das farblose Filtrat ab; dann scheidet das Zinndoppelsalz aus, das man mit verd. Natronlauge behandelt. Die so ausgeschiedene Base wurde mit Äther aufgenommen. Nach Eindampfen des Äthers wurde 1.1 g. Base vom Schmp. 136° erhalten. Nach Umkrystallisieren aus Benzol-Ligroin Schmp. 142.5°. Es stellt etwas rötlich gefärbte, weisse Nadeln dar, welche in Aceton leicht und in Methanol, Äthanol, Äther, Benzol, Toluol und verd. Essigsäure beim Kochen löslich sind, wobei es den Lösungen eine schwach violette Fluoreszenz sich verleiht. (Gef.: N, 9.83. Ber. für $C_{18}H_{16}N_2O_2$: N, 9.58%.)

(8) *m-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäureanilid.* Durch 30 Minuten langes Erhitzen einer Alkohollösung von 0.25 g. Aminokörper (VII) und 0.25 g. *m*-Nitrobenzaldehyd bekam man 0.4 g. Benzylidenverbindung vom Schmp. 216°.

Nach Umkrystallisieren aus Aceton, Schmp. 217.5°, schöne gelbe Nadeln, welche in Aceton, Benzol, Toluol und Essigester beim Kochen leicht löslich und in Methanol, Äthanol und Äther nur ganz wenig löslich sind. In verd. Mineralsäure verseifen sie sich leicht. (Gef.: N, 9.69. Ber. für $C_{25}H_{19}N_3O_4$: N, 9.88%.)

(9) *p-Nitrobenzyliden-(1)-aminonaphthyl-(4)-oxyessigsäureanilid.* Aus 1-Aminonaphthyl-4-oxyessigsäureanilid und *p*-Nitrobenzaldehyd wurde durch einstündiges Kochen ihrer Alkohollösung die entsprechende *p*-Nitrobenzylidenverbindung synthetisiert; goldgelbe Nadeln vom Schmp. 243° aus Aceton. (Gef.: N, 9.89. Ber. für $C_{25}H_{19}N_3O_4$: N, 9.88%.)

(10) *Einwirkung des Schwefelchlorürs auf 1-Aminonaphthyl-4-oxyessigsäure.* In eine Suspension von 2 g. gut getrockneten gepulverten Chlorhydrats der 1-Aminonaphthyl-4-oxyessigsäure (Formel III) in 50 c.c. wasserfreiem Benzol wurden 2 g. Chlorschwefel in 50 c.c. wasserfreiem Benzol innerhalb von 2 Stunden bei 40° getröpfelt. Danach wurde die Temperatur allmählich auf 85° gesteigert. Nach 10 stündigem Erhitzen unter stetigem Umrühren und Luftfeuchtigkeitabschluss wurde das gesamte Gemisch abgekühlt. Man saugt die Niederschläge ab, wäscht mit Benzol aus und trocknet im Vakuum. Die Rohausbeute beträgt 2 g. Dieses Thiazthioniumsalz hat keinen Schmp. und kein Lösungsmittel. Mit Anilin stellt es ein Anilid dar; z.B. werden 4 g. davon in eine Lösung von 6 g. Anilin und 10 g. Eisessig langsam getan. Erst dieses Gemisch löst sich und färbt sich blutrot. Bald aber scheidet das Anilid in goldglänzenden, rotbraunen Blättchen aus. Nach einige Stunden langem Stehenlassen verdünnt man es mit 20 c.c. eines aus 20 c.c. Eisessig, 20 c.c. Wasser und 30 c.c. 2 N Salzsäure bestehenden Säuregemisches, filtriert dies dann ab, wäscht mit dem Säuregemisch aus und trocknet alles im Vakuum über Ätznatron. Die Rohausbeute beträgt 3.5 g. Zur Analyse wurde es aus einem Säuregemisch, das aus 160 c.c. 2 N Salzsäure und 200 c.c. 2 N Eisessig bestand, umkrystallisiert. Aus der anfänglichen Mutterlauge wurde 0.6 g. 1-Aminonaphthyl-4-oxyessigsäure zurückgewonnen. (Gef. für Anilid XII: C, 58.25; H, 3.68; N, 8.62; S, 19.02; Cl, 10,66. Ber. für $C_{16}H_{11}N_2S_2Cl$: C, 58.10; H, 3.33; N, 8.47; S, 19.36; Cl, 10.74%.)

II. **β-Naphthol.** (11) *2-Naphthoxyessigsäure.* Aus 5 g. β-Naphthol und 7 g. Monochloressigsäure in Gegenwart von 27 g. Kalilauge (1 : 2) wurden nach Spitzer[1] 6–7 g. rohe 2-Naphthoxyessigsäure gewonnen. Man löst sie in verd. Ammoniak, verdünnt sie mit

Wasser auf 500 c.c. und filtriert sie. Man schüttelt das Filtrat mit Äther, um das unveränderte β-Naphthol zu trennen. Man säuert die wässerige Lösung mit konz. Salzsäure an, filtriert die abgeschiedenen Niederschläge und wäscht sie mit Wasser. Nach dem Umkrystallisieren aus Wasser wurden 5 g. reine Naphthoxyessigsäure vom Schmp. 156° erhalten. Aus dem Ätherabfalle wurde 0.7–0.8 g. Naphthol zurückgewonnen.

(12) *Einwirkung der Salpetersäure.* 2-Naphthoxyessigsäure wurde ganz genau nach Spitzer nitriert. Man erhält aus 24 g. Oxyessigsäure 26.7 g. rohes Nitroprodukt vom Schmp. 161–181°. Nach 2-maligem Umkristallisieren aus Eisessig zeigte die reine 1-Nitro-2-naphthoxyessigsäure den Schmp. 191–192°. Sie stellt gelbe Nadeln dar, die in Äther und Benzol bei Zimmertemperatur und in Äthanol und Eisessig durch Kochen löslich sind. Es gibt mit Anilin ein Anilid vom Schmp. 169°, Spitzer hat dagegen 139° angegeben.

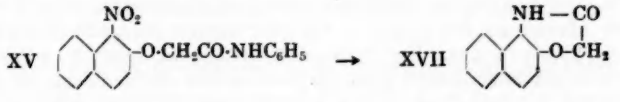
Aus der Mutterlauge beim Umkrystallisieren wurde das zweite Produkt vom Schmp. 157–185°isoliert. Das ist ein isomerer Körper, der ein anderes Anilid vom Schmp. 217° ergibt.

(13) *Anilid des Nitrokörpers.* (A) Durch 10 Minuten langes Erwärmen bei 150–160° einer Lösung von 5 g. 1-Nitronaphthyl-2-oxyessigsäure (Schmp. 185–192°) in 10 g. Anilin wurden 3.9 g. Anilid vom Schmp. 168.5–171° gewonnen. Nach Umkrystallisieren aus Alkohol zeigte die reine 1-Nitronaphthyl-2-oxyessigsäureanilid den Schmp. 169°, was mit dem über Säurechlorid synthetisierten Präparat ganz identisch ist. Sie ist löslich in heissem Äthanol und Anilin. (Gef.: N, 9.00. Ber. für $C_{18}H_{14}O_4N_2$: N, 8.69%.)

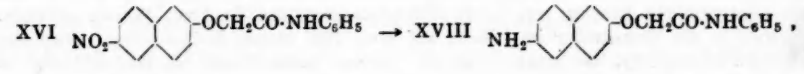
(B) Anderseits wurde durch 20 Minuten langes Erhitzen einer Lösung von 8.2 g. des Produkts vom Schmp. 157–185° in 50 g. Anilin 2.1 g. Anilid vom Schmp. 213–218° erhalten. Nach einmaligem Umkrystallisieren aus Äthanol gab das neue Anilid schwachgelbe, lange Nadeln vom Schmp. 217°. Nach der Analyse ist es auch ein Anilid eines Mononitrokörpers. (Gef.: N, 9.05. Ber. für $C_{18}H_{14}O_4N_2$; N, 8.69%.)

Daraus erhellt dass das zweite Produkt aus einem isomeren Mononitrokörper bestand.

(14) *Reduktion des Anilids.* (A) 2 g. Anilid in 150 c.c. Alkohol wurden mittels 3 g. Zinnpulver und 8 c.c. konz. Salzsäure behandelt. Nach 15 Minuten langem Kochen filtriert man heiss und fügt 100 c.c. Wasser hinzu. Das Produkt wurde mit Äther aufgenommen, nachdem man alles mit Natronlauge alkalinisch gemacht hat. Verdampft man den Äther und krystallisiert den Rückstand aus Äthanol um, so gewinnt man 0.5 g. farblose Nadeln vom Schmp. 218–219°, was mit dem inneren Anhydrid der 1-Aminonaphthyl-2-oxyessigsäure identisch ist (Mischschmelzpunkt). Das Anilid wurde also zerstört.



(B) Aus dem Anilid des isomeren Nitrokörpers konnte man aber in derselben Weise leicht den entsprechenden Aminokörper gewinnen, der aus Alkohol gelbbraune Nadeln vom Schmp. 187–188° darstellt:



wobei die Stellung der NO_2- und der NH_2-Gruppe fraglich ist. (Gef.: N, 9.75. Ber. für $C_{18}H_{16}O_2N_2$: N, 9.58%.)

III. **Schäffersche Säure.** (15) *2-Naphthoxyessig-6-sulfosäure.* Aus 20 g. 2-Naphthol-6-sulfosaurem Natrium, 10 g. Monochloressigsäure, 8.4 c.c. Natronlauge (40° Bé) und 100 c.c. Wasser wurden 22 g. 2-Naphthoxyessig-6-sulfosaures Natrium erhalten, dessen Dihydrat glänzende weisse Tafeln darstellt. (Gef.: Na, 12.60; H_2O (Trocknen beim Xylolsiedepunkt über P_2O_5 in Vakuum), 9.89. Ber. für $C_{12}H_8O_6SNa_2 \cdot 2H_2O$: Na, 12.70; H_2O, 9.94%. Gef. für getrocknete Subst.: Na, 14.04. Ber. für $C_{12}H_8O_6SNa_2$: Na, 14.11%.)

Nach Umkrystallisieren aus verd. Salzsäure erhält man Mononatriumsalz, welches krystallwasserfrei ist. (Gef.: Na, 7.40. Ber. für $C_{12}H_9O_6SNa$: Na, 7.56%.)

(16) *1-Nitronaphthyl-2-oxyessig-6-sulfosäure.*[7] In 15 c.c. Salpetersäure (D = 1.397) wurde 5 g. 2-Naphthoxyessig-6-sulfosaures Natrium bei 20° getan. Nach weiterem 12-stündigen Umrühren bei 15–20° wurden der nitrierten Masse 30 g. Eiswasser zugefügt. Man neutralisiert sie bei Kälte mit etwa 25 c.c. Natronlauge (40° Bé), versetzt sie mit 25 c.c. gesättigter Kochsalzlösung, lässt sie über Nacht stehen und saugt die dann ausgeschiedenen Niederschläge ab. Nach 5-maligem Umkrystallisieren aus Wasser gewinnt man 4 g. 1-Nitrokörper in gelben Nadeln. (Gef.: Na, 12.45; N, 3.62. Ber. für $C_{12}H_7O_8NS\,Na_2$: Na, 12.64; N, 3.77%.)

Ausserdem wurde durch Einengen des von der nitrierten Masse abgesaugten Filtrats 0.7 g. als zweite Ausbeute gewonnen. Nach dem Umkrystallisieren, erst aus verd. Natronlauge, dann 5-mal aus Wasser wurde die Substanz in gelbbrauner Nadeln erhalten. Das ist ein Nebenprodukt, vielleicht 4-Nitrokörper. (Gef.: Na, 12.59; N, 3.51. Ber. für $C_{12}H_7O_8NSNa_2$: Na, 12.64; N, 3.77%.)

(17) *Reduktion des Nitrokörpers.* In ein siedende Lösung von 1 g. Nitrokörper in 0.5 c.c. 20%iger Essigsäure und 2 c.c. Wasser wurde 0.5 g. Eisenpulver getan. Nach 40 Minuten langem Erhitzen wurde alles abgekühlt, mit Natronlauge neutralisiert, nochmals erwärmt und filtriert, worauf 0.8 g. Aminokörper gewonnen wurde. Nach Umkrystallisieren aus Wasser stellt das Produkt etwas rötlich gefärbte Blättchen dar, deren Analyse mit der Zusammensetzung des inneren Anhydrids des erforderlichen Aminokörpers übereinstimmt. (Gef.: Na, 7.52; N, 4.73. Ber. für $C_{12}H_9O_5NSNa$: Na, 7.64; N, 4.65%.)

1 g. Anhydrid wurde in 5 c.c. Natronlauge (40° Bé) und 5 c.c. Wasser gekocht und heissfiltriert. Beim Abkühlen scheidet 1 g. 1-Aminonaphthyl-2-oxyessig-6-sulfosäure in weissen Blättchen aus. Zur Analyse wurde die Substanz einige Male in folgender Weise umkrystallisiert. Man löst die Substanz in einer kleinen Menge Wasser, fügt etwas Natronlauge (40° Bé) hinzu und lässt sie in der Kälte stehen. Man saugt die ausgeschiedenen Krystalle ab und wäscht sie erst mit gesättigter Kochsalzlösung, dann mit Wasser und zuletzt mit Alkohol und trocknet sie. Nach der Analyse entsteht sie aus Dinatriumsalz. (Gef.: Na, 13.15; N, 4.13. Ber. für $C_{12}H_9O_6NSNa_2$: Na, 13.49; N, 4.11%.)

Durch Kochen mit Mineralsäure geht das Natriumsalz wieder in inneres Anhydrid über.

IV. ***Peri-* u. *o*-Dioxynaphthalinsulfosäure.** (18) *1,8-Dioxynaphthalin-3,6-disulfosäure.* 5 g. Chromotropsäure wurden in einer Lösung von 4.3 g. kalz. Soda und 9 c c. Wasser gelöst, worauf man unter Umrühren allmählich innerhalb von etwa 2 Stdn. eine vorher mit Soda neutralisierte Lösung von 1.9 g. Monochloressigsäure in 9 c.c. Wasser tröpfelt, währenddem die Temperatur im Ölbade auf etwa 100° stehen bleiben muss. Nachdem man alles hinzugefügt hat, erhitzt man eine weitere halbe Stunde bei 100° und lässt es

(7) D.R.P. 58614 (Frdl. III. 438).

abkühlen. Man krystallisiert die abgesaugten Krystalle aus verdünnter aus 20 c.c. konz. Salzsäure und 40 c.c. Wasser bestehender Salzsäure um. Die Ausbeute beträgt 2.2 g. weisse Nadeln, welche nach der Analyse Mononatriumsalz der entsprechenden Monooxyessigsäure sind. (Gef.: Na, 5.72; S, 16.01. Ber. für $C_{12}H_9O_{10}S_2Na$: Na, 5.75; S, 16.00%.) Aus der Mutterlauge konnte man 3 g. unveränderte Chromotropsäure zurückgewinnen. (Gef.: Na, 12.28; S, 17.40. Ber. für $C_{10}H_6O_8S_2Na_2$: Na, 12.63; S, 17.60%.)

(19) *Monochloressigsäure auf 1,8-Dioxynaphthalin-4-sulfosäure.* 5 g. Dioxynaphthalinsulfosäure S wurden genau nach Vorschrift (18) behandelt, wodurch man 3 g. grauweisse, rohe Monooxyessigsäure gewann. Nach Umkrystallisieren aus Wasser reine weisse Nadeln. (Gef.: S, 10.64; keine Asche. Ber. für $C_{12}H_{14}O_7S$: S, 10.78%.) Dabei betrug die unveränderte, aus dem Abfall bei der Alkoholwäsche zurückgewonnene Dioxynaphthalinsulfosäure S, 2 g. (Gef.: Na, 6.19; S, 8.84. Ber. für $C_{10}H_7O_5Na_2S \cdot 6H_2O$: Na, 6.21; S, 8.64%.)

(20) *Monochloressigsäure auf 2,3-Dioxynaphthalin-6-sulfosäure.* Durch Behandlung von 5.3 g. 2,3-Dioxynaphthalin-6-sulfosaurem Natron nach Vorschrift (18) wurden 5.5 g. grauweisser Niederschlag gewonnen. Nach Umkrystallisieren aus Wasser 3.8 g. reine 2,3-Dioxyessignaphthalin-6-sulfosäure in weissen Nadeln erhalten. (Gef.: S, 8.38; Na, 6.62. Ber. für $C_{14}H_{11}O_9SNa$: S, 8.46; Na, 6.10%.)

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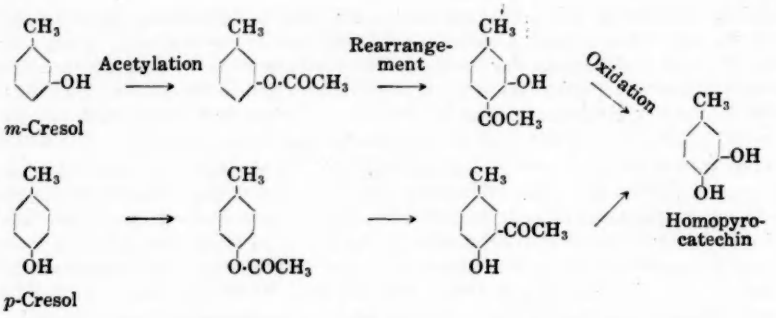
SYNTHESIS OF VANILLIN FROM CRESOLS. I. SYNTHESIS OF HOMOPYROCATECHIN.

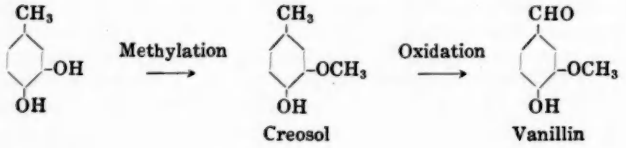
By Kashichi ONO and Minoru IMOTO.

Received October 16th, 1935. Published March 28th, 1936.

The pyrocatechin-derivatives play important rôles in nature as vanillin, adrenalin, urushiol, zingerone, capsaicin, etc. Our factory has succeeded in the industrial preparation of vanillin from safrol, one of the principal constituents of camphor oil, and is now pursuing further studies with a view to a more effective preparation of vanillin and related compounds. This paper concerns the synthesis of homopyrocatechin from cresols. Homopyrocatechin, which has been prepared by the demethylation of creosol, is an intermediate compound of importance for many useful pyrocatechin-derivatives. Our scheme for the synthesis is as follows:



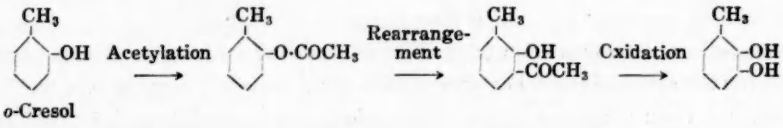
And in addition, the methylation and subsequent oxidation of homopyrocatechin into creosol and vanillin are reported preliminarily.



Through Fries rearrangement of *m*-cresol acetate with aluminium chloride, the acetyl group was rearranged to ortho and para positions to the hydroxyl group.[1] But the ratio of quantities of ortho and para products can be controlled to a certain extent by the conditions. On rearranging at 160°, we obtained 22 g. of *o*-substituted compound and only 2 g. of *p*-substituted. The separation of these is simple, for only the *o*-compound distils with steam. The oxidation of the rearranged *m*-cresyl-methylketone to homopyrocatechin was carried out by the Dakin-process[2] with an alkaline hydrogen peroxide solution.

The case of *p*-cresol, a synthesis completely analogous to the former, is in fact simpler, for the product in Fries rearrangement is an *o*-compound and nothing more.

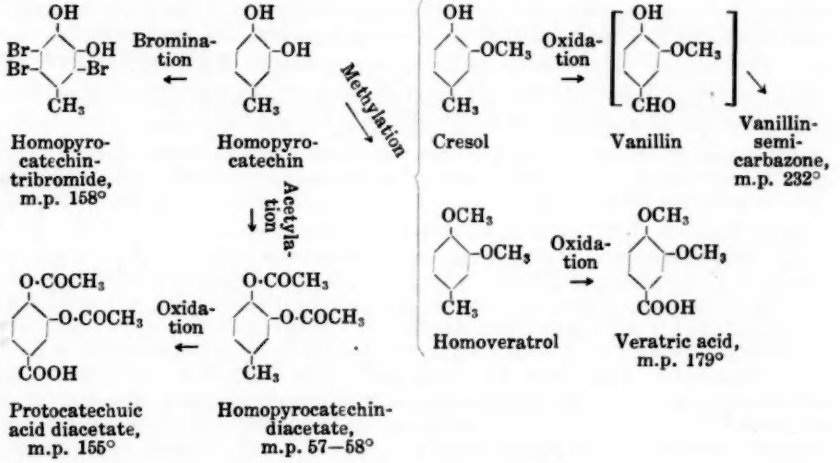
From *o*-cresol, we cannot obtain homopyrocatechin by similar reactions, as the following formulas show :



(1) K.W. Rosenmund and W. Schnurr, *Ann.*, **460** (1928), 56.
(2) H. D. Dakin, *Am. Chem. J.*, **42** (1909), 477.

But fortunately, the *o*-cresyl-methylketone would not give a definite oxidation-product by the Dakin-process, as proved experimentally in our laboratory.[3] And the industrial separation of *o*-cresol from the raw cresol-mixture is possible.[4] So in the preparation of homopyrocatechin according to our method, it is not necessary to use pure cresol, but it is enough that the cresol-mixture is somewhat free from the ortho component.

For the exact identification of the prepared homopyrocatechin, the following derivatives are synthesized :



Of these derivatives, creosol which is obtained from wood-tar, was noted recently as a new material for the vanillin-preparation.[5] And although the oxidation method still remains a subject for future study we have oxidized it preliminarily with ethyl nitrite and obtained vanillin, identifying it as its semicarbazone.

Experimental.

1. **Acetylation of Cresols.** (A) *m-Cresol.* (i) To a solution of *m*-cresol (108 g.), water (70 c.c.), and potassium hydroxide (70 g.), acetic anhydride (110 g.) was added slowly. After washed with 10%-solution of potassium hydroxide, the produced acetate was distilled. Yield, 80% of the theoretical. B.p. 210–215°, n_D^{19} 1.5059, d_4^{15} 1.051. (ii) To a mixture of *m*-cresol (108 g.) and acetic anhydride (130 g.), one drop of conc. sulphuric acid was added.

(3) K. Ono and T. Oyamada, not yet published.
(4) For example, see S. Masai, *J. Soc. Chem. Ind., Japan*, **38** (1935), 217 B.
(5) H. Schulz, *Chem. Ztg.*, **59** (1935), 113.

The temperature was raised, for example, up to 95°. Yield was theoretical. B.p. 210–211°, n_D^{26} 1.4978, d_{26} 1.043.

(B) *p-Cresol.* From 250 g. of *p*-cresol, 300 g. of acetic anhydride, and one drop of conc. sulphuric acid, 280 g. of *p*-cresyl acetate was obtained. B.p. 209–211°, d_{26} 1.043, n_D^{26} 1.4972.

2. **Fries Rearrangement of Acetates.** (A) *m-Cresyl acetate.* To the ice-cooled *m*-cresyl acetate (29 g.), powdered aluminium chloride (30 g.) was added in portions and the mixture heated in an oil-bath at 130°. A violent evolution of HCl gas occurred. Temperature of the oil-bath was raised to 160° during 1.5 hours, and the reaction was then stopped. After cooling, the product was decomposed with ice-water and conc. hydrochloric acid (20 c.c.) and distilled with steam. From the distillate *m*-cresyl-*o*-methylketone was extracted with ether. After redistillation, it weighed 22 g. B.p. 230–235°, n_D^{27} 1.5511, d_{28} 1.081. From the residue of the steam distillation the para product crystallized out. It weighed 2.3 g. and melted at 124–126° after recrystallisation from water.

(B) *p-Cresyl acetate.* Similarly, *p*-cresyl acetate (50 g.) and aluminium chloride (60 g.) gave *p*-cresyl-*o*-methylketone (35 g.), melting at 50° and of somewhat yellowish colour. Recovered acetate weighed 8 g.

3. **Dakin-Oxidation.** (A) *m-Cresyl-o-methylketone.* A solution of *m*-cresyl-*o*-methylketone (22 g.) and sodium hydroxide (7 g.) in water (200 c.c.) was treated with 3% hydrogen peroxide solution at ordinary temperature. As seen from next case, the quantities of NaOH and H_2O_2 (both 1 mole) were insufficient. After standing a whole night, the product was extracted with ether. From the ethereal solution, unchanged *m*-cresyl-*o*-methylketone (15 g.) was recovered by steam distillation. The residue was extracted with ether. After drying the ethereal solution and distilling off the ether, a reddish black oil remained and it yielded a red oil (2.5 g.) boiling at 250-255°. When it was cooled, it solidified. This was the homopyrocatechin somewhat decomposed during the distillation under ordinary pressure.

(B) *p-Cresyl-o-methylketone.* To a solution of *p*-cresyl-*o*-methylketone (11 g.) and sodium hydroxide (7 g., double the theoretical quantity) in water (350 c.c.) was added a 3% hydrogen peroxide solution (260 g., 1.6 times the required quantity). After standing for 3.5 hours, the mixture was acidified with acetic acid and the unchanged *p*-cresyl-*o*-methylketone was distilled off with steam. It weighed 2 g. By extraction and redistillation there was obtained a somewhat yellowish, viscid, oily homopyrocatechin, boiling at 122° (6 mm.), 117° (4 mm.) or 114° (3 mm.). In the receiver, the oil solidified into a white, mass, but when left in the air, it became a red liquid again. (Found: C, 67.17; H, 6.76. Calc. for $C_7H_8O_2$: C, 67.74; H, 6.50%.)

(C) *Homopyrocatechin-tetrabromide.* A bromide was prepared according to H. Cousin.[6] To a solution of homopyrocatechin in glacial acetic acid was dropped a solution of bromine in the same solvent. Hydrogen bromide was evolved. After 1.5 hours, water was added. The separated substance was recrystallized repeatedly from dil. acetic acid. Somewhat orange coloured needles were obtained, m.p. 158° (Cousin gives m.p. 162–163°). (Found: C, 22.75, 23.73; H, 1.88 Calc. for $C_7H_5O_2Br_3$: C, 23.27; H, 1.38%.)

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(6) H. Cousin, *Ann. chim.*, (7), **13** (1898), 480.

(D) *Homopyrocatechin-diacetate.* After heating at 140–150° a mixture of homopyrocatechin (3 g.), acetic anhydride (10 g.), and anhydrous sodium acetate (2 g.) for four hours, the contents were extracted with ether, the ethereal solution washed with 10% KOH and fractionated under ordinary pressure. The obtained diacetate was a somewhat yellowish oil, boiling at 274–275°[7] and having the following constants: n_D^{28} 1.4932, d_4^{28} 1.1314 and M.R. 53.44 (theoretical 52.71). On standing, it solidified and it melted at 57–58° after recrystallisation from alcohol. (Found: C, 63.38, 63.02; H, 6.10, 6.09. Calc. for $C_{11}H_{12}O_4$: C, 63.46; H, 5.78%.)

(E) *Oxidation of the homopyrocatechin-diacetate.* The diacetate (0.2 g.), mixed with 0.5 N sulphuric acid (20 c.c.), was oxidized with 2% potassium permanganate on the water-bath. The obtained diacetate of protocatechuic acid melted at 143°. After double recrystallisation from water, it was identified with the diacetate of protocatechuic acid[8] by the mixed melting point.

4. **Methylation and Oxidation of Homopyrocatechin.** A mixture of homopyrocatechin (4.5 g.), caustic potash (6 g.), water (30 c.c.), and impure sodium methylsulphate (9 g.) was refluxed for 2.5 hours. Then the contents were dissolved in water, and the dimethylated ether (homoveratrol) was extracted with ether. The residue was acidified with dil. hydrochloric acid and the monomethylated ether (creosol) was extracted with ether.

(A) Homoveratrol, weighing 1.0 g., was obtained as yellowish oil from the ethereal solution. B.p. 216–218°, n_D^{28} 1.5250, d_4^{29} 1.051 (Found: M.R. 44.29; C, 70.66; H, 7.99. Calc. for $C_7H_{12}O_2F_3$: M.R. 43.65; C, 71.05; H, 7.90%). For the identification, the homoveratrol was oxidized with 2.5% potassium permanganate. It gave veratric acid, melting at 179°.

(B) Creosol was obtained as yellowish oil. It weighed 1.2 g. and smelled somewhat of guaiacol. B.p. 218–225°, n_D^{27} 1.5347, d_4^{27} 1.100.

(C) *Oxidation of Creosol.* Ethyl nitrite, prepared from sodium nitrite (2.5 g.), alcohol, and sulphuric acid by Wallach's method,[9] was passed into the solution of creosol (0.3 g.) in alcohol (0.5 g.) cooled with ice and salt. NO_2-gas evolved. The contents became reddish-dark and some white precipitates were produced. After filtration and extraction of the filtrate with ether, the ether was evaporated off and the resulting tarry residue was extracted with hot water. To the water extract were added semicarbazide hydrochloride (0.1 g.), potassium acetate (0.1 g.), and alcohol (1 c.c.). On the next day, crystals of the resulting semicarbazone separated, were collected. M.p. 220–225°. After recrystallisation it melted at 227–229°, and proved to be vanillin-semicarbazone by the mixed melting point.

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(7) Cousin gives b.p. 264°.

(8) M. Imoto, *J. Chem. Soc. Japan*, **55** (1934), 523.

(9) O. Wallach, *Ann.*, **245** (1889), 251. M. Imoto, *J. Chem. Soc. Japan*, **55** (1934), 120.

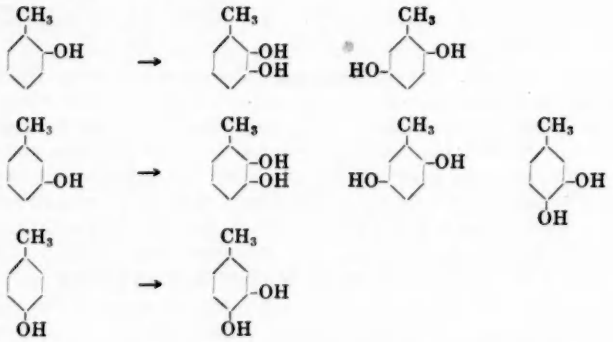
ON THE REACTION BETWEEN CRESOLS AND HYDROGEN PEROXIDE IN THE PRESENCE OF FERROUS SULPHATE.

By Kashichi ONO and Taichiro OYAMADA.

Received October 16th, 1935. Published March 28th, 1936.

In 1900, Caross, Bevan, and Heiberg[1] reported that benzene when oxidised with hydrogen peroxide in the presence of ferrous sulphate yielded phenol (15%) and pyrocatechin (35%). Though this reaction seems to be interesting from the standpoint of pure chemistry as well as applied chemistry, only a few investigations on this subject have hitherto been carried out.[2]

The present authors extended this reaction to three isomeric cresols with the view to examining whether the direct introduction of a hydroxyl-group into a benzene nucleus is possible as in the case of benzene itself. If this reaction is always the case, it is expected that the following compounds, which are all important not only from a scientific, but also from a technological point of view, can be obtained :



As shown in details in the experimental part, the oxidation of *o*-cresol with hydrogen peroxide in the presence of ferrous sulphate was first conducted under various conditions and the chief product of the oxidation was a black substance, which is insoluble in water, partly soluble in ether and, on combusting, leaves iron oxide. Besides this substance *p*-toluhydroquinone

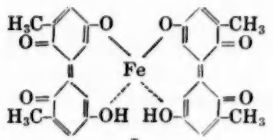
(1) *Ber.*, **33** (1900), 2015.

(2) Sommer, D.R.P. 155731. Bargellini and Monti, *Gazz. chim. ital.*, **45** (1915), 90. O. Magidson and N. Preobrashenski, *Trans. Sci.-Chem.-Pharm. Inst.* (*Moscow*), **16** (1926), 65.

was isolated in a small amount. Although some attempts were made to separate oxidation products, the oxidation products turned out to be nothing more than the above-mentioned substances, and the expected 1-methyl-2,3-dihydroxybenzene was not isolated.

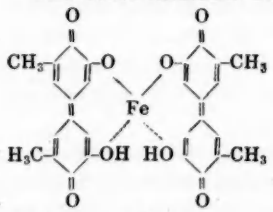
Now it is necessary to investigate the nature of this black substance in order to make clear the whole reaction. But, owing to the difficulty in purifying this substance, it was impossible to obtain a complete elucidation. After long and fruitless trials, however, it was found to be most probably a mixture of three or more substances. First, it was separated into an ether-soluble and an ether-insoluble parts. The ether-soluble part was separated into two compounds by gradual addition of petroleum ether. The precipitate first formed was represented by composition $C_{28}H_{22}O_8Fe$. On reduction with zinc dust and HCl in alcoholic solution, it gave a colourless compound melting at 202°, which was further converted into its acetate, melting at 135°, by heating with acetic anhydride and fused sodium acetate. This acetate was proved to be 2,5,2′,5′-tetracetoxy-3,3′-dimethyl-diphenyl by elementary analysis and mixed melting point test. Consequently, the reduction product which melts at 202° may be 2,5,2′,5′-tetrahydroxy-3,3′-dimethyl-diphenyl because of agreement in melting point and composition. From these results, it follows that the compound represented by $C_{28}H_{22}O_8Fe$ is probably a complex of Fe with two mol ditolydiquinone, represented by formula I.

The precipitate formed last was a yellow crystalline powder melting at 163–5° and found to be ditolydiquinone by analysis. Moreover, this was also ascertained to be the case by converting it into 2,5,2′,5′-teracetoxy-3,3′-dimethyl-diphenyl by means of reductive acetylation.



I

The ether-insoluble black substance was also represented by formula $C_{28}H_{22}O_8Fe$ (although the analytical data was unsatisfactory) and, on reductive acetylation, gave an acetate melting at 194–6° in a small amount. On the other hand, Prof. Majima,[3] in his series of researches on urushiol, tried to oxidise 1-methyl-2,3-dihydroxybenzene with $FeCl_3$ and then observed the formation of a complex compound (II).



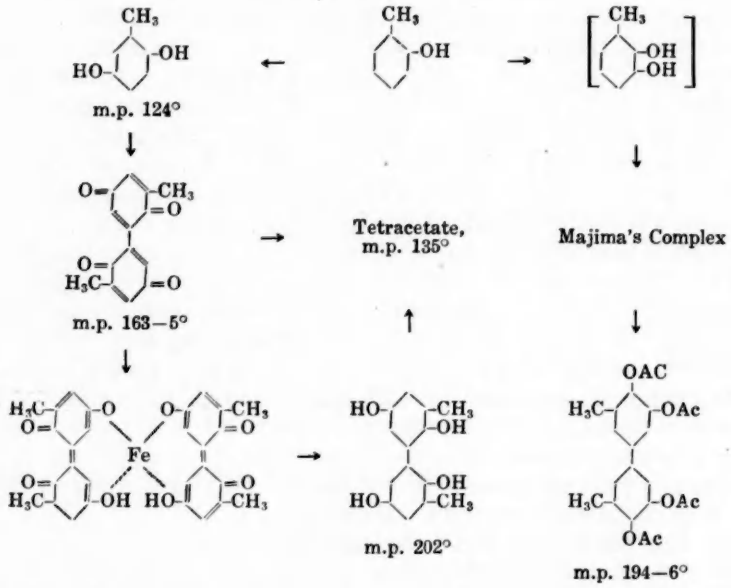
II

The complex obtained by the present authors seems to be in agreement with Majima's complex in appearance, composition, and the melting point of

(3) *Ber.*, **53** (1920), 1907.

the reductively acetylated product, so they may be assumed to be in all probability the same compound. Thus, 1-methyl-2,3-dihydroxybenzene which could not be isolated may be considered to have once been formed and to have undergone subsequent oxidation and condensation.

The above-described results can be summarised in the following manner:



Such a direct introduction of the hydroxyl-group into the benzene nucleus has been demonstrated already in the case of the anodic oxidation of aromatic compounds by various investigators. For instance, F. Fichter and Franz Ackermann[4] obtained *p*-toluhydroquinone and 4,4′-dihydroxy-3,3′-dimethyldiphenyl from *o*-cresol by anodic oxidation. It is of interest to note that the oxidation with H_2O_2 in the presence of $FeSO_4$ takes place in a manner somewhat similar to that of electrolytic oxidation.

Under the same conditions as described above *m*- and *p*-cresols were oxidised. In the former case, a large amount of a black substance together with a little *p*-toluhydroquinone was isolated as in the case of *o*-cresol, and the black substance, on close examination, was proved to be a mixture of ditolydiquinone and a complex containing Fe. From the oxidation products of

(4) *Helv. Chim. Acta*, **2** (1919), 596.

p-cresol, no definite crystalline compound except a black substance was isolated. This black substance was treated in the same way as in the case of *o*-cresol. From the ether soluble part, on reductive acetylation, an acetate which melts at 145° was obtained but owing to the small quantity, a further investigation could not be carried out. From the ether insoluble part, on reduction and subsequent acetylation, an acetate melting at 250° was obtained which also could not be identified owing to the scarcity of the substance.

Experimental Part.

I. **Oxidation of *o*-cresol with H_2O_2 in the presence of $FeSO_4$.** (a) To a mixture of 40 g. of *o*-cresol and 100 c.c. of water containing 6 g. of $FeSO_4$, 300 c.c. of 2% aqueous solution of H_2O_2 was added in portions with frequent shaking and the mixture was allowed to stand overnight, when the solution became brownish red and a black resinous oil separated out. In order to drive off unacted cresol the whole oxidised mixture was subjected to steam distillation and 19 g. of *o*-cresol was obtained from the distillate. On cooling, a resinous mass solidified in the residue of the steam treatment and was collected on a filter. The filtrate separated from the black substance was thoroughly extracted with ether and then the ethereal solution evaporated, when about 2.5 g. of a reddish substance remained and gradually crystallised which was dried on a porous plate and recrystallised from benzene. It forms colourless needles melting at 124° and was identified with *p*-toluhydroquinone by elementary analysis and mixed melting point test. (Found: C, 67.68; H, 6.86. Calc. for $C_7H_8O_2$: C, 67.8; H, 6.4%.)

(b) To a mixture of 40 g. of *o*-cresol and 100 c.c. of water containing 10 g. of $FeSO_4$, 300 c.c. of 2% aqueous hydrogen peroxide solution was added drop by drop with ice-cooling and vigorous stirring. After being allowed to stand for several hours at room temperature, the excess of H_2O_2 was decomposed by the addition of MnO_2. With the intention of isolating the expected 1-methyl 2,3-dihydroxybenzene, the whole mixture was first treated with a solution of lead acetate when a brown precipitate of a lead salt was deposited. The precipitate thus obtained was washed with water, alcohol, and ether succesively, decomposed with dilute sulphuric acid, and extracted with ether. From the ethereal extract a brown resinous matter was obtained, from which no definite compound could be isolated. The mixture was treated with lead acetate solution, mixed together with the washings and submitted to steam distillation, and 25 g. of unchanged *o*-cresol was recovered. The residue was filtered from the black viscous resinous matter and extracted with ether. From the ethereal solution *p*-toluhydroquinone was obtained in a small amount. The aqueous solution which had been treated with ether was evaporated to dryness under reduced pressure, from which no definite organic compound was isolated.

(c) To a mixture of 30 g. of *o*-cresol and 100 c.c. water containing 6 g. of $FeSO_4$, 300 c.c. of 2% aqueous hydrogen peroxide solution was added in small portions and the temperature was maintained at 80° during the oxidation.

The investigation of oxidation products was carried out just as in case (a) and about 1 g. *p*-toluhydroquinone and a large amount of the black material were obtained.

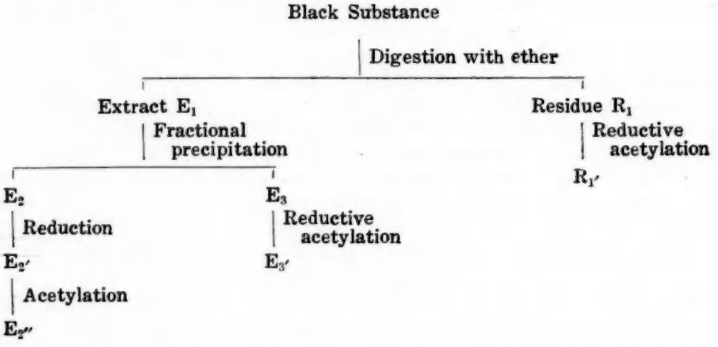
(d) A solution of 30 g. of *o*-cresol in acetone was mixed with a solution of ferrous sulphate in 100 c.c. water and the mixture heated with constant stirring on the water-bath. Three hundred c.c. of 2% aqueous solution of H_2O_2 was added to the mixture

drop by drop. From the oxidation products nothing other than the above-mentioned materials was isolated.

(e) When a large amount of $FeSO_4$ was used, the chief oxidation product was obtained as a black powder instead of an oily substance. Aside from this, *p*-toluhydroquinone was found in a small amount as in the above cases.

To a mixture of 30 g. of *o*-cresol and 100 c.c. of water containing 40 g. of $FeSO_4$, 300 c.c. of 2% aqueous solution of H_2O_2 was added in portions with vigorous shaking. Twenty grams of a black substance and 2 g. of *p*-toluhydroquinone were obtained from the oxidation products.

II. **The investigation of the black substance.** As already stated, the chief oxidation product was a black substance insoluble in water. For a further investigation of this substance, it was treated as follows:



Of course, a complete separation was by no means attained in this way, but it was possible to speculate that it would be a mixture of the substances described in the introduction.

(A) *Part soluble in ether.* The black substance was thoroughly extracted with ether in a Soxhlet apparatus. On addition of petroleum ether to the ethereal solution, E_2 first and then E_3 separated out.

(a) *Complex salt* (E_2). E_2 was again dissolved in ether and fractionally reprecipitated by addition of petroleum ether. By the repetition of this process, E_2 was purified and used in a further experiment as below. (Found: C, 61.05; H, 5.13; Fe, 9.67. Calc. for $C_{28}H_{22}O_8Fe$: C, 61.99; H, 4.06; Fe, 10.14%.)

(b) *Reduction of* E_2 ($E_{2'}$). To a mixture of 1 g. of E_2 in alcohol (20 c.c.) and 5 g. of zinc dust, 5 c.c. of concentrated HCl was slowly added. After an hour, the reaction mixture was filtered by suction and the solution was poured into 150 c.c. of cold water, when an almost colourless precipitate separated out. It was recrystallised from alcohol, crystalline powder melting at 202°, and giving data agreeing with 2,5,2′,5′-tetrahydroxy-3,3′-dimethyl-diphenyl. (Found: C, 68.03; H, 6.10. Calc. for $C_{14}H_{14}O_4$: C, 68.29; H, 5.69%.)

(c) *Acetylation of* $E_{2'}$ ($E_{2''}$). One gram of $E_{2'}$ was boiled with 10 c.c. of acetic anhydride together with 2 g. fused sodium acetate under reflux for an hour. After cooling, it was poured into cold water, when a colourless precipitate separated out.

The precipitate was recrystallised from alcohol, a colourless crystalline substance melting at 135° and showing no depression of melting point by admixture with 2,5,2′,5′-tetra-acetoxy-3,3′-dimethyl-diphenyl synthesized from *p*-toluhydroquinone. (Found: C, 63.56; H, 6.10. Calc. for $C_{22}H_{22}O_8$: C, 63.8; H, 5.3%.)

(d) *Purification of* E_3. E_3 was also dissolved in ether and petroleum ether was added until a yellow precipitate was just separating out. To the filtrate a large amount of petroleum ether was added to complete the precipitation, when a yellow substance was deposited. By repeating such a treatment several times, a yellow crystalline powder melting at 163-5° was obtained. The analytical data and the melting point agree with those of ditolydiquinone. This was, moreover, ascertained also by converting it into its acetate. (Found: C, 68.98; H, 4.68. Calc. for $C_{14}H_{10}O_4$: C, 69.42; H, 4.13%.)

(e) *Reductive acetylation of* E_3. Two grams of E_3 was dissolved in 15 c.c. of acetic anhydride and 5 g. of zinc dust and 3 g. of fused sodium acetate were added and the whole was boiled under reflux for an hour, when the brownish red colour of the initial mixture faded. After removal of the excess of zinc dust, the mixture was poured into cold water and left to stand. A yellowish mass separating out therefrom, and after recrystallisation from alcohol it showed a melting point 135°, agreeing with the data for 2,5,2′,5′-tetracetoxy-3,3′-dimethyl-diphenyl. It was moreover identified by the mixed melting point test with a synthetical specimen which had been prepared by the reductive acetylation of ditolydiquinone, prepared from *p*-toluhydroquinone according to Brunner.

(B) *Part insoluble in ether* (R_1). (a) *Reductive acetylation of* R_1. Twelve grams of R_1 was boiled with 20 c.c. of acetic anhydride together with 14 g. of fused sodium acetate and 10 g. of zinc dust under reflux for an hour. While hot, excess of zinc was filtered off and the solution thus obtained was poured into cold water, when a yellowish mass separated. On recrystallisation from alcohol, a colourless substance melting at 193-5° was obtained. This melting point coincides with that of 3,3′-dimethyl-4,4′,5,5′-tetracetoxy-diphenyl. (Found: C, 61.25; H, 5.20; Fe, 9.56. Calc. for $C_{28}H_{22}O_8Fe$: C, 61.99; H, 4.06; Fe, 10.14%.)

III. **Oxidation of *m*-cresol with H_2O_2 in the presence of $FeSO_4$.** Thirty grams of *m*-cresol was oxidised under the same conditions as in case (a) for *o*-cresol. The formation of *p*-toluhydroquinone and the black material were also observed here. The investigation of the black material was carried out exactly in the same way as in the case of *o*-cresol. (A) *Part soluble in ether.* By the treatment as in the case of *o*-cresol, ditolydiquinone and the complex of Fe with it were detected. (B) *Part insoluble in ether.* From this part, no definite compound could be isolated.

IV. **Oxidation of *p*-cresol with H_2O_2 in the presence of $FeSO_4$.** The oxidation and the separation of the resulting products were carried out as in the above two cases. (A) *Part soluble in ether.* On reductive acetylation by means of acetic anhydride and zinc dust, it gave an acetate melting at 145° in a very small amount. (B) *Part insoluble in ether.* By reductive acetylation, an acetate melting at 250° was obtained in a small amount. These two acetates could not be identified owing to the small amounts of the substances available.

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STUDIES ON AMINO-ACIDS AND RELATED COMPOUNDS. IX. ELECTROLYTIC OXIDATION OF PROLINE AND γ-AMINO-BUTYRIC ACID.

By Yoshitaro TAKAYAMA.

Received October 18th, 1935. Published March 28th, 1936.

In a previous paper[1] it was reported briefly that the electrolytic oxidation of proline may proceed in a type similar to that of pyrrolidone-carboxylic acid. In this paper the details of the above oxidation and that of γ-amino-butyric acid are reported.

Langheld[2] oxidized *dl*-proline with sodium hypochlorite and isolated a certain base having an odour of pyrrolidine. Recently Herbst and Clark[3] treated proline with silver oxide, but no definite compound was obtained.

In the present experiment, proline in dilute sulphuric acid was electrolyzed in an undivided cell with a lead peroxide anode and a lead cathode under the following conditions: current quantity about 8F./mol; temperature 35°C.

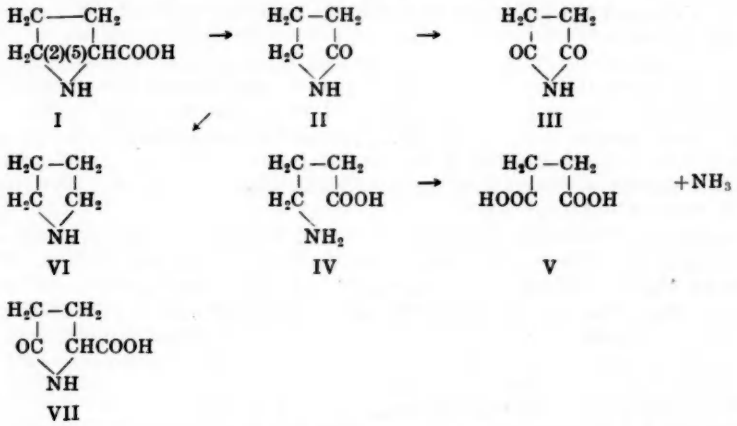
In the electrolysate, no substance giving aldehydic reaction could be found. By thorough extraction with ether it was divided into two parts. The part soluble in ether was found to consist of a comparatively large amount of succinimide together with a little succinic acid. From the residual part, by treating with barium hydroxide, ammonia as well as pyrrolidine were isolated as volatile bases. The pyrrolidine was confirmed by the analysis of its chloroplatinate and by the formation of characteristic precipitates on addition of a solution of potassium bismuth iodide.

In the solution, from which volatile bases were removed, there was found some amount of amino-nitrogen, which greatly increased when the solution was boiled with barium hydroxide and, in fact, γ-amino-butyric acid was isolated in the form of its chloroplatinate. It may be a proper reasoning to consider that the above increase of amino-nitrogen means an accumulation of γ-amino-butyric acid due to the hydrolysis of pyrrolidone[4], though, in reality, the base itself was not isolated.

The electrolytic oxidation of γ-amino-butyric acid was carried out just in the same manner as described above and from its electrolysate ammonia, succinic acid, and unchanged amino-acid were isolated.

(1) Y. Takayama, this Bulletin, **8** (1933), 213.
(2) K. Langheld, *Ber.*, **42** (1909), 2373.
(3) R. M. Herbst and H. T. Clark, *J. Biol. Chem.*, **104** (1934), 769.
(4) J. Tafel and M. Stern, *Ber.*, **33** (1900), 2230.

Taking the two sets of oxidation into consideration, the mechanism of electrolytic oxidation of proline may be represented as follows:



Proline (I) was first oxidized to pyrrolidone (II) and the latter, on further oxidation, gives succinimide (III) and this course of reaction seems to be a main one, when interpreted from the amount of the final products. γ-Amino-butyric acid (IV) as well as pyrrolidine (VI) are presumed to be derived from pyrrolidone, the former by hydrolysis, the latter by reduction. As to the formation of succinic acid (V) two possible processes can be conceived: hydrolysis of succinimide and oxidation of γ-amino-butyric acid.

It was shown by E. Fischer[5] that proline can be formed by the reduction of pyrrolidone-carboxylic acid (VII). In the present oxidation, as a matter of fact, not pyrrolidone-carboxylic acid[6] but γ-amino-butyric acid together with pyrrolidine was obtained, thus, the reverse of the E. Fischer's reaction can not be imagined to occur in this case. It naturally leads to the conclusion that the carbon atom (5) in proline is more readily oxidizable than the carbon atom (2).

Experimental Part.

Electrolytic Oxidation of Proline. Proline (Fraenkel and Landau) m.p. 209–210° after recrystallization from *n*-butyl alcohol.

The above sample (1.151 g., 10 millimols) was dissolved in N sulphuric acid (27 c.c.) and electrolyzed under the following conditions: cell the same as described in part VII[7];

(5) E. Fischer, *Ber.*, **44** (1911), 1332.
(6) Y. Takayama, this Bulletin, **8** (1933), 137.
(7) Y. Takayama, this Bulletin, **8** (1933), 213.

electrodes (2 cm. × 4 cm.) PbO_2–Pb; current density 2 amp./dm^2.; 3.5 volts; current quantity 8 F./mol; temperature 35°C.

The electrolysate of proline (10 millimols × 2) was thoroughly extracted with ether. Ether was expelled, and the remaining crystalline mass was separated into neutral and acidic parts as usual.

Neutral part (*succinimide*). Crystals (0.5 g.) obtained were recrystallized from acetone, m.p. 126°. It was found to be succinimide by the determination of nitrogen as well as by the mixed melting point test (Found: N, 14.2. Calc. for $C_4H_5O_2N$: N, 14.15%).

Acidic part (*succinic acid*). Crystals (0.2 g.) obtained melted at 183° after recrystallization from water. It was identified as succinic acid by the determination of acid equivalent and mixed melting point test (4.419 mg. of this acid required 5.56 c.c. (0.01346 N NaOH). Calc. for $C_4H_6O_4$: 5.63 c.c.).

Volatile bases (*ammonia and pyrrolidine*). After removal of the part soluble in ether from the electrolysate, the residual solution was distilled with an excess of barium hydroxide under reduced pressure, the volatile bases being collected in dilute hydrochloric acid. On evaporating up the solution, a very hygroscopic crystalline mass was obtained, which was treated with absolute alcohol, and were separated into soluble and insoluble parts.

The hydrochloride (0.1 g.) insoluble in alcohol was found to be ammonium chloride by the analysis of its chloroplatinate and by the inspection of crystal forms under polarizing microscope (Found: Pt, 43.9. Calc. for $(NH_4)_2PtCl_6$: Pt, 43.96%).

On expelling the solvent from the hydrochloride solution very hygroscopic crystals were obtained, which was subjected to steam distillation with sodium hydroxide. The distillate was shaken with an excess of yellow mercuric oxide[8] and filtered. After twice repeating the above treatments, the solution was distilled with steam. The free base thus obtained gave no reaction of pyrrole, it gave the characteristic crystalline precipitates of pyrrolidine when a solution of potassium bismuth iodide was added. The chloroplatinate of this base crystallized in orange rods (straight extinction), which decomposed at 210°. The result of the analysis coincided with that of chloroplatinate of pyrrolidine (Found: Pt, 35.4. Calc. for $(C_4H_9N)_2H_2PtCl_6$: Pt, 35.34%).

Separation of γ-Amino-butyric Acid. After removal of part soluble in ether and volatile bases from the electrolysate, the solution was treated with CO_2, to remove the large bulk of barium. The filtrate was concentrated under reduced pressure, and boiled with an excess of barium hydroxide. The solution, after complete removal of barium, was extracted with ether. From the ethereal extract a small quantity of succinic acid (m.p. 183°) was obtained, which remained unextracted in the previous treatments.

In the residual solution, 1.63 mg. of amino-nitrogen (74.3% of total-nitrogen) was found and it gave an intense ninhydrin reaction. From this solution yellow crystalline chloroplatinate (0.13 g.) was isolated which, after recrystallization, decomposed at 220°. It was identified as γ-amino-butyric acid by the decomposition point and by the comparison of crystalline behaviours under polarizing microscope (straight extinction, sign of elongation: negative) with those of synthetic sample. The hydrochloride of this base was prepared from the chloroplatinate, as usual, and it gave an intense ninhydrin reaction. Here again its behaviours under polarizing microscope coincided with those of synthetic hydrochloride.

To assertain the nitrogen distribution and the presence of pyrrolidone in the electrolysate, proline (0.707 g.) was electrolyzed (7.9 F./mol) under the same conditions as already

(8) E. Abderhalden, "Handbuch der biologischen Arbeitsmethoden," 1923, I, 7, 347.

described. The volatile bases (NH_3, pyrrolidine) and barium were removed from the electrolysate, and the amounts of amino-nitrogen as well as total nitrogen in the solution were determined. After boiling with an excess of barium hydroxide for two hours, the amounts of the two forms of nitrogen in it were again determined. The amount of amino-nitrogen (percentage to total nitrogen) reached 93.9% after this treatment, the net increase exceeding 20%.

Oxidation of γ-Amino-butyric Acid. γ-Amino-butyric acid[9] was prepared by the electrolytic reduction of succinimide. It melted at 203° with decomposition (Found : N, 13.5. Calc. for $C_4H_9O_2N$: N, 13.59%. Found : Pt, 31.6. Calc. for $(C_4H_9O_2N)_2H_2PtCl_6$: Pt, 31.62%).

γ-Amino-butyric acid (1.031 g., 10 millimols) in N H_2SO_4 (27 c.c.) was electrolyzed, current quantity being 8.25 F./mol, under the same conditions as in the case of proline. Amino-N/total-N in the electrolysate was 30.28%. The electrolysate was extracted thoroughly with ether. Succinic acid (0.2 g.) was obtained from the ethereal extract and it was recrystallized from water, which melted at 183°. The acid equivalent and silver content in its silver salt were determined (29.6 mg. acid required 5.00 c.c. (0.09972 N NaOH). Calc. for $C_4H_6O_4$: 5.02 c.c. Found : Ag, 64.8. Calc. for $C_4H_4O_4Ag_2$: Ag, 65.04%).

The residue of the ethereal extraction was treated with $Ba(OH)_2$, and ammonium chloride was isolated as volatile base (Found : Pt, 43.7. Calc. for $(NH_4)_2PtCl_6$: Pt, 43.93%). After the removal of succinic acid, ammonia, and barium from the electrolysate, unchanged γ-amino-butyric acid was recovered in crystalline form (m.p. 203°).

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SYNTHESIS OF β,γ-DIHYDROXY-PROPYL-GUANIDINE.

By Sin'iti KAWAI and Noboru SUGIYAMA.

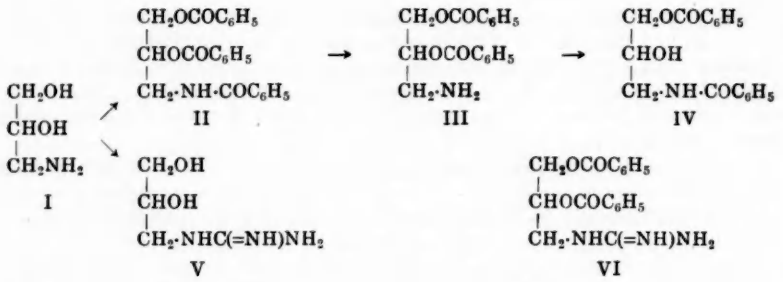
Received October 25th, 1935. Published March 28th, 1936.

One of us (K.) has synthesized β-hydroxy-ethyl-guanidine[1]. Polyhydroxy-alkyl-guanidine, as we are aware, seems not yet been described in the literature. With the object of enlarging our knowledge upon the synthetic methods of polyhydroxy-alkyl-guanidine we attempted to synthesize β,γ-dihydroxy-propyl-guanidine, on which will be briefly reported here.

Starting from glycerol we first obtained amino-propylene glycol (I).

(9) J. Tafel and M. Stern, *Ber.*, **33** (1900), 2224.

(1) S. Kawai, *Sci. Pap. Inst. Phys. Chem. Research, Japan*, **16** (1931), 24.



Amino-propylene glycol was benzoylated to its tribenzoyl-derivative (II) from which one benzoyl group was removed to *O,O'*-dibenzoyl-γ-amino-propylene glycol (III)[2]. *O,O'*-Dibenzoyl-γ-amino-propylene glycol hydrochloride (III) and an equivalent quantity of cyanamide were heated at 120–130°C in a sealed tube, absolute alcohol, or anhydrous pyridine being chosen as the solvents. In both cases, instead of procuring the expected β,γ-dibenzoyl-propyl-guanidine (VI), the reaction proceeded in an unexpected manner, and the sole crystalline product which we gained was the *O,N*-dibenzoyl-γ-amino-propylene glycol of Bergmann (IV)[3]. When we submitted *O*-methyl-pseudo-urea (free base) to reaction in place of cyanamide, the result was the same. In all cases the reactions ended in the acyl displacement from oxygen to nitrogen.

Our trial to synthesize β,γ-dihydroxy-propyl guanidine (V) succeeded, however, when we applied free amino-propylene glycol (I) and *S*-methyl-pseudo-thiourea hydroiodide as the starting materials. The β,γ-dihydroxy-propyl-guanidine (V) was isolated and identified as its picrate.

Experimental.

Amino-propylene glycol (I). Glycerol-α-monochlorhydrin was first synthesized after R. Adams[4], which was transformed into glycidol[5]. The latter was converted to amino-propylene glycol[6] (b.p. 163–165°/18 mm.) with concentrated aqueous ammonia.

O,N-dibenzoyl-γ-amino-propylene glycol (IV). Only one case will be written here for simplification. Into a sodium methylate solution (from 0.5 g. of metallic sodium and 5 c.c. of absolute methyl alcohol), which was cooled with ice water from outside, an absolute methyl alcoholic solution (10 c.c.) of *O*-methyl-pseudo-urea hydrochloride[7] (2.4 g.)

(2) M. Bergmann, *Ber.*, **54** (1921), 936.
(3) *Loc. cit.*
(4) R. Adams, "Organic Synthesis," II, 33.
(5) J.U. Nef, *Ann.*, **335** (1904), 231. T.H. Rider, *J. Am. Chem. Soc.*, **52** (1930), 1521.
(6) L. Knorr and E. Knorr, *Ber.*, **32** (1899), 752.
(7) J. Stieglitz, *Ber.*, **33** (1900), 1517.

was slowly added. After standing for about an hour, the separated sodium chloride was filtered off. Into this filtered solution *O,O'*-dibenzoyl-γ-amino-propylene glycol hydrochloride (III)[8] (7.28 g.) was added and the whole was shaken until dissolution was complete, temperature not being raised above 30°C.

After standing overnight the solution was concentrated to about two-thirds of its original volume under reduced pressure. Two days later the separated crystals were sucked off and were recrystallized several times from aqueous methyl alcohol. Colourless long plates, m.p. 108–109°C. Judging from its melting po nt and the analytical results no doubt can be inserted in its identity with the Bergmann's *O,N*-dibenzoyl-γ-amino-propylene glycol. Bergmann gives m.p. 109°C (corr.). (Found : C, 68.14, 67.99; H, 5.61, 5.69; N, 4.67, 4.50. Calc. for $C_{17}H_{17}O_4N$: C, 68.20; H, 5.73; N, 4.68%.)

β,γ-Dihydroxy-propyl-guanidine (V). Into an alcoholic solution (10 c.c.) of amino-propylene glycol (0.91 g., $^1/_{100}$ mol) *S*-methyl-pseudo-thiourea hydroiodide (2.18 g., $^1/_{100}$ mol) was added and the whole was refluxed on a steam bath for about 1.5 hours, strong evolution of mercaptan being observed. When the major part of the solvent was driven off under reduced pressure from the reaction mixture we obtained a syrupy mass, which showed no sign of crystallization even though it was kept in a vacuum desiccator for several days.

The syrup, however, exhibits positive colour-reactions of guanidine and it can be concluded that β,γ-dihydroxy-propyl guanidine hydroiodide was produced, in spite of its non-crystallizing tendency, which is presumably originated in its hygroscopic nature. The attempt to isolate the hydroiodide was then abandoned and the syrupy material was treated with a concentrated aqueous solution of sodium picrate (2.5 g.). Yellow crystals soon separated, which were collected. Yield 1.45 g. The picrate thus obtained was recrystallized several times from water. M.p. 126°C. Yellow fine prisms.

As is shown in the following analytical data, as well as the positive colour-reactions of guanidine (Sakaguchi's test, carmine red; Weber's test, blood red) it can be concluded that β,γ-dihydroxy-propyl-guanidine picrate was obtained. (Found : C,33.26, 33.55; H, 3.71, 4.04; N, 22.89, 22.83[9]. Calc. for $C_{10}H_{14}O_9N_6$: C, 33.13; H, 3.90; N, 23.20%.)

The authors wish to express their hearty thanks to Prof. R. Majima for his kind advice.

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(8) M. Bergmann, *loc. cit.*

(9) The nitrogen analysis of guanidine derivative, arginine for instance, often shows too small amount of nitrogen.

4,5-BIS-(*m*-AMINOPHENYL)-CARBAZOLE.

By Shin-ichi SAKO.

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This investigation was undertaken with a view to elucidate the spatial relations of the two phenyl nuclei contained in 4,5-diphenyl-carbazole. Although the work has not so far progressed as was originally intended, it has been thought advisable, for the reasons which will be given at the end of this introduction, to communicate some of the results already obtained.

In a previous paper[1], a brief account was given of the structure of 4,5-diphenyl-carbazole. It was there stated that, as the two phenyl nuclei cannot occupy their normal positions owing to the collision with each other, the valencies carrying the phenyl groups will have to be in a strained condition. Assuming that the atoms of the carbazole nucleus lie in a single plane[2], and taking into account that the molecule would assume the least strained form possible in the circumstances, it was suggested that the most probable structure representing the substance would be one in which the two phenyl nuclei lie in planes approximately perpendicular to the plane in which the carbazole nucleus lies. This is shown by Fig. 1, which is constructed on the assumption that the interatomic distances, C–C and C–N, is approximately 1.42 Å and also that valency distortion is possible only in the same planes as those in which the benzene nuclei lie. The thick lines indicate the sides of hexagons which are nearer to the reader. The directions of the valencies carrying the phenyl groups are those when the two carbon atoms of the *p*-positions of the phenyl nuclei are in mutual contact with the interatomic distance 1.42 Å, in other words, when the angle α is 125.1°. Since, however, it is inconceivable that the two atoms which is not in actual combination should be in such close proximity, actually the angle α will be somewhat larger than this. At any rate, this figure serves to indicate that, when the molecule assumes the structure represented by Fig. 1, the intramolecular strain is not large. The

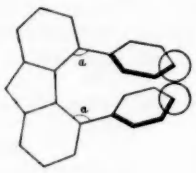


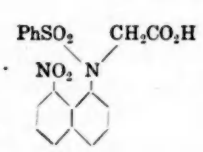
Fig. 1.

(1) Sako, this Bulletin, **9** (1934), 63.

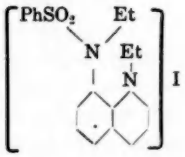
(2) That the carbazole nucleus has a coplanar configuration has been shown by the fact that when *d*- or *l*-2,2′-diamino-1,1′-dinaphthyl is heated with HCl, inactive naphthocarbazole is produced (Kuhn and Goldfinger, *Ann.*, **470** (1929), 183). See also Adams and Yuan, *Chem. Rev.*, **12** (1933), 289.

facile formation of 4,5-diphenyl-carbazole[3] from 2,2′-diamino-6,6′-diphenyl-diphenyl and also of 4,5-bis-(*m*-aminophenyl)-carbazole (XV) from 2,2′-diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV) may be attributed to this cause.

If Fig. 1 represents the stable form of 4,5-diphenyl-carbazole, a question which is naturally raised is whether or not there is a possibility of the rotation of the two phenyl nuclei around the bond carrying them. The observations such as those by Mills and his co-workers that benzenesulphonyl-8-nitronaphthylglycine (I)[4] and 8 benzenesulphonylethylamino-1-ethyl-quinolinium iodide (II)[5] can be obtained in optically active forms and the resolvability of many of the ortho-substituted diphenyl compounds due to the restricted rotation of the two nuclei seem to indicate that the rotation of the phenyl nuclei of 4,5-diphenyl-carbazole should also be restricted in a similar manner. The probability that the rotation of one of the phenyl groups will be obstructed by the other is perhaps more clearly indicated in the diagrammatical representation of this compound given in Fig. 2, which is constructed on the assumption



I



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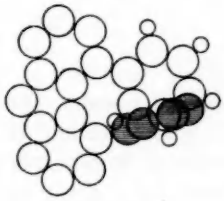


Fig. 2.

that the atoms of carbon and nitrogen may be regarded as spheres of a diameter approximately 1.42 Å, and that the hydrogen atoms as spheres of a diameter approximately one half of the diameter of the carbon atom. The carbazole nucleus is shown in the left half of the figure, and the hydrogen-atoms attached to this nucleus are omitted to simplify the diagram. The six carbon atoms of one of the phenyl groups, which are assumed to lie in the same plane as that in which the carbazole nucleus lies, are indicated in the upper-right of the figure, and the small spheres attached to five of these carbon atoms represent the hydrogen atoms[6]. The horizontally shaded spheres

(3) Sako, this Bulletin, **9** (1934), 70.

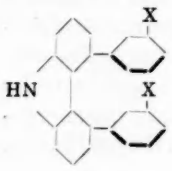
(4) Mills and Elliot, *J. Chem. Soc.*, **1928**, 1291.

(5) Mills and Breckenridge, *J. Chem. Soc.*, **1932**, 2209.

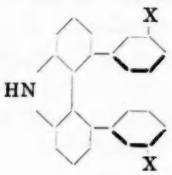
(6) That the hydrogen atoms in the nucleus do act as obstacles and are not embedded in the nuclear carbon atoms has been proved by the fact that diphenyl with only two substituents of proper size in opposite nuclei is resolvable (Turner and his co-workers, *J. Chem. Soc.*, **1932**, 2021, 2394; *ibid.*, **1933**, 135. Searle and Adams, *J. Am. Chem. Soc.*, **55** (1933), 1649. See also *Chem. Soc. Annual Reports*, **1933**, p. 258).

represent the four of the six carbon atoms of the other phenyl group which are assumed to be lying in a plane perpendicular to the plane of the paper. The positions of the two phenyl nuclei indicated in the figure are those when they are in their supposed normal positions.

It will be seen that, for the rotation of one of the phenyl nuclei by sweeping the obstacles presented by the other, the molecule will have to be distorted very considerably, the magnitude of this distortion being perhaps comparable to, if not larger than, that required in the case of the compounds I and II examined by Mills and his co-workers. The compound should therefore be represented by the structure given in Fig. 1, which appears to be the least strained condition of the molecule attainable in the circumstances. If the rotation of the phenyl nuclei are in fact thus limited, it follows that a 4,5-diphenyl-carbazole derivative, which contains each of a substituent in the meta- (or ortho-) positions of the two phenyl nuclei, should exist in a pair of geometrical isomers, one cis and the other trans, as shown respectively by the formulæ IIIa and IIIb, and that, since the transform (IIIb) does not possess a plane of symmetry, it should exist in two enantiomorphous modifications.



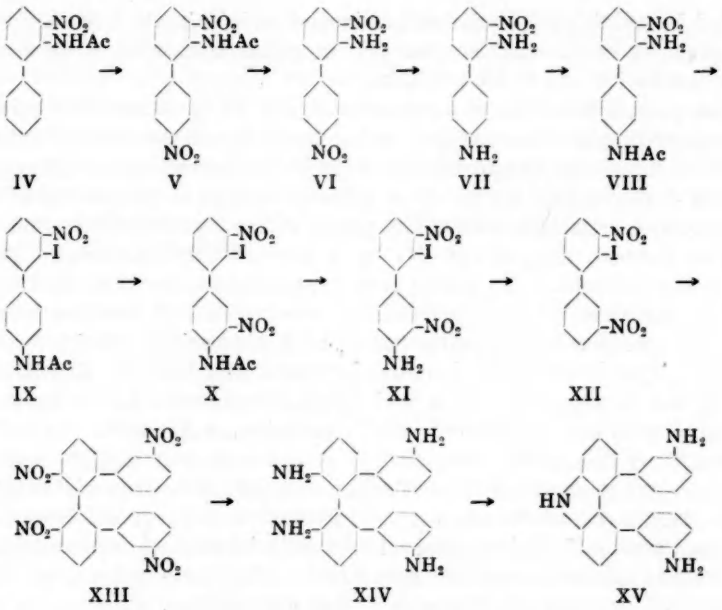
III a



III b

It seemed therefore that the simplest way to test those views stated above experimentally would be through the examination of such a type of 4,5-diphenyl-carbazole derivative as indicated by formulæ IIIa and IIIb. The compound which was selected for examination was 4,5-bis-(*m*-aminophenyl)-carbazole (XV) which has been obtained in the following way. 3-Nitro-2-acetamidodiphenyl (IV), which has been prepared through a series of processes from diphenyl by Sako's method[7], can be successively converted into 3,4′-dinitro-2-acetamidodiphenyl (V), 3,4′-dinitro-2-amino-diphenyl (VI), 3-nitro-2,4′-diaminodiphenyl (VII), 3-nitro-2-amino-4′-acetamidodiphenyl (VIII), 2-iodo 3-nitro-4′-acetamidodiphenyl (IX), 2-iodo-3,3′-dinitro-4′-acetamidodiphenyl (X), 2-iodo-3,3′-dinitro-4′-aminodiphenyl (XI), 2-iodo-3,3′-dinitrodiphenyl (XII), and the latter treated according to the Ullmann method with copper powder. 2,2′-Dinitro-6,6′-bis-(*m*-nitrophenyl)-diphenyl(XIII), produced in this way, on reduction, passes into 2,2′-diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV), which, upon heating with HCl, yields 4,5-bis (*m*-aminophenyl)-carbazole (XV):

(7) This Bulletin, **9** (1934), 65.



Scarborough and Waters[8] have found that, although it contains the acetamido-group which tends to promote substitution in the same nucleus, 2-acetamidodiphenyl is nitrated in the 4′-position in the presence of acetic acid and conc. H_2SO_4, 4′-nitro-2-acetamidodiphenyl being obtained in a good yield[9]. This anomalous behaviour must be attributed to the presence of conc. H_2SO_4 which in general weakens, most probably due to the salt formation, the directive influence of the acetamido-group. This view is supported by the fact that when nitrated in the presence of acetic acid alone, 2-acetamidodiphenyl affords the 5-nitro-derivative[10] as the primary product. From these facts and also from the fact that 3-nitro-2-acetamidodiphenyl (IV) contains the nitro-group which tends to prevent substitution from occurring in the same ring, it is to be expected that the compound IV, when nitrated in the presence of conc. H_2SO_4 and acetic acid, should give mainly 3,4′-dinitro-2-acetamidodiphenyl (V). The experiment fully justified this expectation, for it has been found that under the conditions the compound (V) is produced in 73% yield. A conclusive proof of the position of the entering nitro-group has been

(8) *J. Chem. Soc.*, **1927**, 95.
(9) Sako, this Bulletin, **10** (1935), 585.
(10) Bell, *J. Chem. Soc.*, **1928**, 2773.

afforded by oxidizing 3,4′-dinitro-2-aminodiphenyl (VI), which is obtained by the hydrolysis of V, with chromic acid in acetic acid, when *p*-nitrobenzoic acid is obtained as one of the products.

The partial reduction of compounds V and VI, and 2-iodo-3,4′-dinitrodiphenyl, with sodium sulphide of which the latter can be obtained from VI by the usual method, was attempted in the hope of effecting the reduction of only the 4′-nitro-group contained in these substances. As a matter of fact, however, the partial reduction of compound VI has been found to be the only workable method, the yield of VII being 89% of the theoretical. That a nitro-group adjacent to an amino-group resists reduction with an alkaline sulphide has already been observed in the case of *o*-nitroaniline which is recovered unchanged after being heated with ammonium sulphide[11]. This behaviour of *o*-nitro-aniline is in marked contrast with that of *o*-nitro-acetanilide, of which compound V is a derivative, for under similar conditions the acetylated base can be reduced with ammonium sulphide[12]. As will be foreseen from this, when compound V was treated with sodium sulphide, both nitro-groups appeared to be attacked, and the chance of partial reduction taking place in the desired manner only seemed remote. It has been found that when 2-iodo-3,4′-dinitro-diphenyl is heated with alcoholic sodium sulphide, the resulting substance contains no halogen. This observation is in accord with that of Beilstein and Kurbatow[13] that the reaction, which occurs when *o*-chloronitro-compounds such as 1-chloro-2,4-dinitrobenzene are heated with $(NH_4)_2S$, K_2S, or better with KSH, is the elimination of halogen.

In the monoacetylation of 3-nitro-2,4′-diaminodiphenyl (VII), advantage was taken of the fact that the amino-group adjacent to the nitro- and also to the phenyl group is not attacked by acetic anhydride, the theoretical yield of the monoacetylated product VIII being obtained easily. This was a matter which had been anticipated, for it had been known that 3,5-dinitro-2-aminodiphenyl[14] and 3-nitro-2-aminodiphenyl[15], which, like compound VII, have each a nitro- and a phenyl-group in positions adjacent to the amino-group, cannot be acetylated even by boiling with acetic anhydride.

2-Iodo-3-nitro-4′-acetamidodiphenyl (IX), on nitration with nitric acid of D. 1.45–1.46, yields dinitro-compound X, but with nitric acid of D. 1.51–1.52, the trinitro-compound, 2′-iodo-3,5,3′-trinitro-4-acetamidodiphenyl (XVI). The constitution of this dinitro-compound (X) follows from the following considera-

(11) *Ber.*, **25** (1892), 987.

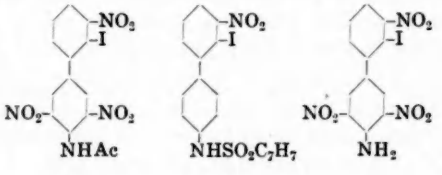
(12) Lassar-Cohn, " Arbeitsmethoden f. org. Chem. Lab.", 5 Ed., p. 861 ; cf. Niementowski, *Ber.*, **43** (1910), 3024.

(13) *Ber.*, **11** (1878), 2056.

(14) Bell, *J. Chem. Soc.*, **1928**, 2774.

(15) Sako, this Bulletin, **9** (1934), 68.

tions: (i) since there is a nitro-group in one of the nuclei of IX, the second nitro-group would naturally go to the other nucleus containing the acetamido-group which tends to promote substitution, and this should be more so as the nitration was conducted in the presence of nitric acid alone; (ii) that the compound appears to be a derivative of *o*-nitroacetanilide and not that of *m*-nitroacetanilide has been shown by the fact that free base (XI) obtained by its hydrolysis does not form the hydrochloride in a dil. HCl solution, and also that the deamination of the free base (XI) through the diazonium salt resulting in 2-iodo-3,3′-dinitrodiphenyl (XII) takes place with utmost readiness; (iii) by the nitration of 2-iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl (XVII), a product is obtained, which, on hydrolysis, yields a trinitroamino-compound identical with that obtained by the hydrolysis of the trinitroacetamido-compound (XVI). In view of the very powerful ortho-para-directing influence exerted by the *p*-toluenesulphonamido-group as has been shown by Bell[16], the most probable structure of this trinitro-amine would be formula XVIII.



XVI XVII XVIII

There was no difficulty presented in the preparations of 2,2′-dinitro-6,6′-bis-(*m*-nitrophenyl)-diphenyl (XIII), 2,2′-diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV), and 4,5-bis-(*m*-aminophenyl)-carbazole (XV). The free base of the latter crystallized, however, with difficulty. This property, coupled with the fact that it is rather readily oxidized in the air, rendered obtaining the free base XV in pure crystalline condition impossible. The hydrochloride and the diacetyl derivative of XV could be obtained readily in a state of purity. The sharp melting point possessed by this diacetyl compound indicated that it was a single substance, but since compound XV has been produced at such a high temperature as over 200° in the presence of HCl, it is possible that the more stable form (probably the trans form (IIIb)) alone is produced.

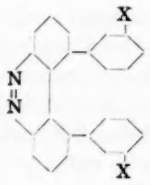
Attempts to resolve compound XV with *d*-camphor-sulphonic acid and *d*-tartaric acid have not been successful. The former acid gave no crystalline salt, and, although the latter acid gave a difficultly soluble tartarate in alcohol, the deep brown colour of this salt rendered the polarimetric examination impossible. This colour was undoubtedly caused by the oxidation in the air, which appeared to occur more readily when the base exists as a salt than when it is free. On account of this property and also of the small quantity

(16) *J. Chem. Soc.*, **1928**, 2770.

of the material (XV), a detailed examination of these salts had to be postponed till a later date (as already stated, for the synthesis of XV, no fewer than fifteen stages of preparations are required).

Compound XV was then submitted to the action of *l*-menthoxyacetyl chloride, when the stable 4,5-bis-(*m*-*l*-menthoxyacetamidophenyl)-carbazole was obtained in 73% yield. Its sharp melting point indicated that the *l*-menthoxyacetyl derivative was a single substance, although it does not necessarily follow from the good yield that the bis-(aminophenyl)-carbazole portion of the *l*-menthoxyacetyl compound is optically inactive, since there is a possibility that the substance might have been obtained as a result of processes of optical activation, similar to those observed, for example, by Pope and Peachy[17] with methyl-ethyl-*n*-propyl-tin-*d*-camphor-sulphonate, by Mills and Elliot[4] with the brucine salt of benzenesulphonyl-8-nitro-naphthyl-glycine, and by Yuan and Adams with the brucine salt of 2′-nitro-2,5-dimethoxydiphenyl-6′-carboxylic acid. Unfortunately, however, attempts to eliminate the *l*-menthoxyacetyl group by means of hydrolysis have so far been failures. That the rotation of an active substance is greatly influenced by the nature of solvents has been demonstrated once again by the bis-*l*-menthoxyacetyl derivative of XV. Thus, although it has $[\alpha]_D$ −22.27° in EtOH and −24.65° in acetone, the sign of rotation is completely reversed in benzene, in which $[\alpha]_D$ is +14.2°.

Although, owing to lack of material, the behaviour of the active acids on XV has not been examined so thoroughly as otherwise would have been possible, it seemed that the rather unstable nature of XV and its salts was unsuited or at least not advantageous for the investigation of this kind. It is proposed, therefore, to investigate the matter in other compounds of similar type which fulfil the conditions mentioned above, including, if possible, those containing a 6-membered ring in place of the 5-membered ring of XV, such as, for example, shown in formula XIX. From similar considerations regarding the probability of restriction of rotation of the phenyl groups, it is apparent that, since XIX should be more highly strained than XV, the rotation of the phenyl groups will be more difficult in XIX than in XV.



XIX

Experimental.

3,4′-Dinitro-2-acetamidodiphenyl (V). A solution of 42.8 g. of 3-nitro-2-acetamidodiphenyl in 85 c.c. each of glacial acetic acid and conc. H_2SO_4 was cooled with ice and

(17) *J. Chem. Soc., Proc.*, **16** (1900), 12, 42, 116.

treated gradually with a mixture of 8.6 c c. of fuming HNO_3 of D. 1.52, 15 c.c. of glacial acetic acid, and 15 c.c. of conc. H_2SO_4 with constant stirring, the mixed acids being added at such a rate that the temperature of the reaction mixture was maintained below +2°. After the mixed acids had been added, stirring was continued one more hour. The mixture was then poured on ice, and the precipitated so id collected. The dried crude product weighed 49.2 g. It was dissolved in 1600 c.c. of boiling EtOH and left overnight. The yellow crystals (30.5 g.) thus separated were almost pure 3,4′-dinitro-2-acetamidodiphenyl (V). By concentration of the mother liquor, somewhat impure crystals were obtained, which on recrystallization gave a second crop (6.4 g.). The yield of V was therefore 73% of the theoretical. Pure 3,4′-dinitro-2-acetamidodiphenyl had m.p. 207.5° with previous sintering (Found : N, 14.2. Calc. for $C_{14}H_{11}O_5N_3$: N, 14.0%).

The mother liquors separated from the main product, on further concentration, deposited more soluble nitration products in crystalline condition, but they have not been investigated so far. 3,4′-Dinitro-2-acetamidodiphenyl (V), when treated with alcoholic sodium sulphide, yielded a product which contained at least two substances, one yellow and the other red, the latter being identified with compound VII by the mixed melting point method.

3,4′-Dinitro-2-amino-diphenyl (VI). 3,4′-Dinitro-2-acetamidodiphenyl (V) (37 g.) was refluxed with a mixture of 450 c.c. each of EtOH and conc. HCl on the water bath for 7 hours. The free base separated as orange needles during the heating. After cooling, the product (31.1 g.) was collected, dried, dissolved in 900 c.c. of boiling benzene, and the solution allowed to cool. The orange leaflets thus obtained, 28 g., melted at 196–197° (Found : N, 16.5. Calc. for $C_{12}H_9O_4N_3$: N, 16.2%).

The dinitroamino-compound (VI),. on oxidation with chromic anhydride in acetic acid, gave *p*-nitrobenzoic acid as one of the products, showing that in the nitration of IV, the second nitro-group entered the 4′-position : a suspension of 3,4′-dinitro-2-aminodiphenyl in 10 parts of glacial acetic acid was treated with 5 parts of chromic anhydride with agitation. The substance disappeared with the evolution of heat, forming a dark-green, thick liquid. After standing for some hours, it was diluted with water, when a yellow precipitate separated. It was collected, dissolved in dil. ammonia solution and some insoluble matter was filtered off. The filtrate, on acidifying with HCl, deposited a yellow crystalline solid, which, on recrystallization, gave yellow crystals, which showed no depression of the melting point when mixed with the authentic specimen of *p*-nitrobenzoic acid.

2-Iodo-3,4′-dinitrodiphenyl. 3,4′-Dinitro-2-aminodiphenyl (VI) (1.3 g.) was dissolved in 5 c.c. of conc. H_2SO_4 at ordinary temperature. The vessel was then surrounded by ice, and 3.5 g. of cracked ice and 0.38 g. of powdered sodium nitrite were added with stirring. After a time, 2.5 g. of ice was added and stirring continued for an hour. A large quantity of ice was then added, and some suspended matter removed by filtration. The filtrate, on addition of 1.0 g. of KI, decomposed at once, the iodo-compound being precipitated. It was dissolved in ether, and the ethereal solution was shaken with a KOH solution and dried. On removal of the ether, a crystalline solid remained, which after being treated with animal charcoal in alcohol, was twice crystallized from the solvent (50 c.c.). It formed yellow, flat needles melting at 139–140° (Found : I, 34.33. Calc. for $C_{12}H_7O_4N_2I$: I, 34.31%). The yield was 1.4 g.

In an attempt to effect the partial reduction of the 4′-nitro-group only, the iodo-dinitro-compound was treated with sodium sulphide in EtOH and a small quantity of

water, when fine needles separated, which contained no halogen. This product has not been studied.

3-Nitro-2,4′-diaminodiphenyl (VII). The procedure described below for the partial reduction of 3,4′-dinitro-2-aminodiphenyl (VI) is the outcome of a number of comparative experiments which were made to determine the best conditions. A suspension of 26 g. of 3,4′-dinitro-2-amino-diphenyl (VI) in 600 c.c. of EtOH was mixed with a solution of 40 g. of $Na_2S \cdot 9H_2O$ in 150 c.c. of water, and refluxed on the boiling water bath for an hour. The original substance disappeared in a quarter of an hour, forming a red solution. After the requisite time, the hot solution was diluted with 250 c.c. of water, when 3-nitro-2,4′-diaminodiphenyl (VII) separated immediately in crystalline state. The red crystals were collected, washed with EtOH–H_2O, and dried. The substance thus obtained was almost pure, had m.p. 156–157°, and may be used for a further experiment. The yield was 20.5 g. or 89.1% of the theoretical. On crystallization from EtOH, it gave red crystals melting at 157° (Found : N, 18.6. Calc. for $C_{12}H_{11}O_2N_3$: N, 18.3%).

3-Nitro-2-amino-4′-acetamidodiphenyl (VIII). Acetic anhydride (6.9 g.) dissolved in a few c c. of benzene was added to a suspension of 13.8 g. of 3-nitro-2.4′-diaminodiphenyl (VII) in 80 c.c. of benzene. The reaction commenced to occur at once, but it was heated on the boiling water bath for 30 minutes, during which time the original red crystals were replaced by the yellow crystals of the acetyl compound (VIII), which is practically insoluble in benzene. 3-Nitro-2-amino-4′-acetamidodiphenyl (VIII) thus obtained was pure and had m.p. 174–175° (Found : N, 15.80. Calc. for $C_{14}H_{13}O_3N_3$: N, 15.50%). The yield was 16.2 g. (theoretical).

2-Iodo-3-nitro 4′-acetamidodiphenyl (IX). 3-Nitro-2-amino-4′-acetamidodiphenyl (VIII) (17.4 g.) was added in small portions to 77 c.c. of conc. H_2SO_4 at ordinary temperature with agitation. The resulting clear solution was cooled with ice water, treated with 60 g. of ice and then with 5.0 g. of NO_2Na which was added during 30 minutes. As soon as the thick foam had subsided, a large quantity of ice was added, and the red solution thus obtained treated with a solution of 14 g. of KI in the cold. Shortly afterwards, a vigorous reaction took place. External heating was not necessary, as the decomposition was complete even in the ice-cold temperature. The precipitated product was filtered and washed successively with a $Na_2S_2O_3$ solution and water. The dried crude product weighed 24.5 g. It was dissolved in 2240 c.c. of boiling alcohol and allowed to stand for crystallization. The yellow leaflets thus obtained melted at 239° with previous softening (Found : I, 33.1. Calc. for $C_{14}H_{11}O_3N_2I$: I, 33.2%). The yield of the pure substance was 22 g. or 90% of the theoretical.

2-Iodo-3-nitro-4′-aminodiphenyl and its hydrochloride. A suspension of 1.9 g. of 2-iodo-3-nitro-4′-acetamidodiphenyl (IX) in a mixture of 20 c.c. each of alcohol and conc. HCl was refluxed on the water bath for 1.5 hours during which time the original crystals were replaced by the yellow crystals of the hydrochloride of 2-iodo-3-nitro-4′-aminodiphenyl. After cooling, it was collected, washed with EtOH–conc. HCl and then with ether (Found : Cl, 9.32. Calc. for $C_{12}H_9O_2N_2I \cdot HCl$: Cl, 9.42%.). The yield of the hydrochloride was 1.8 g. It can be crystallized from water.

To obtain the free base, the hydrochloride obtained above was shaken with an excess of NaOH solution and ether, and the upper layer, after being dried with K_2CO_3, evaporated up. The residual crystals, on crystallization from EtOH, gave yellow crystals melting at 126–127° (Found : I, 37.16. Calc. for $C_{12}H_9O_2N_2I$: I, 37.33%).

2-Iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl (XVII). To a solution of 1.12 g. of 2-iodo-3-nitro-4′-aminodiphenyl in 3 c.c. of pyridine was added 0.66 g. of *p*-toluenesulphonyl chloride, and the reddish solution thus obtained was heated on the water bath until the colour had almost disappeared. It was then diluted with water and shaken with benzene. The benzene solution, when shaken with a $CaCl_2$ solution, separated a gummy material which solidified on rubbing. On crystallization from EtOH, 2-iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl separated as beautiful yellow, transparent crystals which melted at 136–137° (Found I, 25.44; S, 6.56. Calc. for $C_{19}H_{15}O_4N_2IS$: I, 25.69; S, 6.49%).

2-Iodo-3,3′-dinitro-4′-acetamidodiphenyl (X). At first, the preparation of this compound from 2-iodo-3-nitro-4′-acetamidodiphenyl (IX) presented unexpected difficulties, and it was only after a large number of comparative experiments, in which nitric acid of varied concentrations was employed, that this compound (X) became obtainable in an almost theoretical yield. The success of the nitration depended essentially upon the concentration of nitric acid, according to which either the dinitro-compound (X) or the trinitro-compound (XVI) was obtained exclusively.

To 40 c.c. of nitric acid of D. 1.456 which was cooled with ice water, was gradually added 7.64 g. of 2-iodo-3-nitro-4′-acetamidodiphenyl (IX) with stirring. The substance disappeared almost instantaneously after each addition. The addition of the original substance took about one hour, and the agitation was continued one more hour. Some of the product separated towards the end of the reaction. Reaction mixture was then poured into ice, and the solid thus appeared collected. The dried crude product weighed 8.6 g. On crystallization from 615 c.c. of EtOH, it formed yellow leaflets melting at 196–197° (Found: N, 10.11. Calc. for $C_{14}H_{10}O_5N_3I$: N, 9.84%). The yield of the purified substance was 8 g. or 93.7% of the theoretical.

2-Iodo-3,3′-dinitro-4′-aminodiphenyl (XI). A suspension of 7.26 g. of powdered 2-iodo-3,3′-dinitro-4′-acetamidodiphenyl (X) in a mixture of 100 c.c. each of EtOH and conc. HCl was refluxed on the water bath for 1.5–2.0 hours. Fifty c.c. of water was then added to the hot mixture, and the crystalline product thus separated filtered after cooling. The substance (6.5 g.) was the almost pure free base (XI). Crystallized from EtOH, it formed yellow needles which melted at 178–178.5° (Found: N, 11.22, Calc. for $C_{12}H_8O_4N_3I$: N, 10.91%).

2′-Iodo-3,5,3′-trinitro-4-acetamidodiphenyl (XVI). 2-Iodo-3-nitro-4′-acetamidodiphenyl (IX) (0.57 g.) was added during 15 minutes and with stirring to 6 c.c. of fuming HNO_3 of D. 1.52 which was cooled in an ice bath. After a short time (it has been found essential that the reaction mixture should be poured into ice without delay, for otherwise an amorphous product would result, from which no crystalline substance can be isolated), the reaction mixture was poured on ice and the yellow solid thus separated collected and dried. It was dissolved in 300 c.c. of boiling EtOH and the solution, after being concentrated, left overnight. The crystals thus obtained, on one more crystallization from EtOH, yielded slightly yellow needles melting at 263–264° (Found: N, 11.96. Calc. for $C_{14}H_9O_7N_4I$: 11.86%). The yield of the pure substance was 0.4 g.

2′-Iodo-3,5,3′-trinitro-4-aminodiphenyl (XVIII). This base was obtained by the hydrolysis of 2′-iodo-3,5,3′-trinitro-4-acetamidodiphenyl (XVI) and also of the product obtained by nitrating 2-iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl (XVII).

A mixture of 2′-iodo-3,5,3′-trinitro-4-acetamidodiphenyl (XVI), conc. HCl and EtOH was refluxed on the water bath for a long time. The free base began to appear when

there was still a considerable quantity of the original acetyl compound left unaffected in the reaction mixture. The base was purified by crystallization from EtOH, from which it separated as yellow thin needles melting at 220–221° (Found : N, 13.12. Calc. for $C_{12}H_7O_6N_4I$: N, 13.02%). It is readily soluble in cold benzene.

The same base was also obtained from 2-iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl as follows. 2-Iodo-3-nitro-4′-*p*-toluenesulphonamidodiphenyl (XVII) (0.25 g.) was added in small portions to 0.5 c.c. of fuming HNO_3 of D. 1.51 at ordinary temperature with agitation. After some time, water was added and the precipitated product filtered off. The product, 0.29 g., after crystallization from EtOH, was dissolved in 1 c.c. of conc. H_2SO_4 by gentle heating, and the solution, after cooling, poured into water. The yellow precipitate thus obtained, on crystallization from EtOH, gave yellow needles which melted, either alone or when mixed with the base obtained by the hydrolysis of the acetyl compound (XVI), at 220–221°.

2-Iodo-3,3′-dinitrodiphenyl (XII). 2-Iodo-3,3′-dinitro-4′-aminodiphenyl (XI) (6.6 g.) was added slowly to 28 c.c. of conc. H_2SO_4 at ordinary temperature with constant stirring, and the stirring continued until the substance had disappeared (1.5 hours). With continued stirring and with cooling with ice water, it was treated with 19 g. of ice and then 1.4 g. of NO_2Na, the latter being added in small portions. After an hour, 9 g. of ice was added and stirring continued for some time. The reaction mixture was then added gradually to 280 c.c. of boiling EtOH and the solution, after being refluxed on the water bath for an hour, filtered while hot to remove a trace of the red byproduct which was deposited during the reaction. The clear filtrate was concentrated, diluted with water, and the precipitate thus obtained extracted with ether. The ether was then removed, when 6.3 g. of the crystalline product was left behind, which, on vacuum distillation, gave 6.0 g. of the distillate boiling at 239°/6 mm. Upon crystallization from EtOH, 2-iodo-3,3′-dinitrodiphenyl separated in beautiful yellow needles which melted at 130–131° (Found : N, 7.72. Calc. for $C_{12}H_7O_4N_2I$: N, 7.57%).

2,2′-Dinitro-6,6′-bis-(*m*-nitrophenyl)-diphenyl (XIII). Copper powder (1.27 g.) was added during 4 minutes to 3.70 g. of well-stirred 2-iodo-3,3′-dinitrodiphenyl (XII) which was heated in an oil bath at 190–195°. After the copper powder had been added, the heating was continued for 5 to 7 minutes more, during which time the mass solidified completely. The product was extracted with a large quantity of boiling benzene, and the blue benzene extract shaken with water to remove the colour which was due probably to the presence of a copper compound. The benzene was then evaporated off, and the yellow residue (2.35 g.) crystallized from glacial acetic acid. 2,2′-Dinitro-6,6′-bis-(*m*-nitro-phenyl)-diphenyl thus obtained was yellow needles melting at 259.5–260° (Found : N, 11.70 Calc. for $C_{24}H_{14}O_8N_4$: N, 11.52%.) The yield of the pure substance was 90.5% of the theoretical. Compound XIII was not so easily soluble in cold benzene, but once dissolved by heating, it did not crystallize from this solvent even when it was greatly concentrated. One gram of it dissolves in about 55 c.c. of boiling acetic acid.

2,2′-Diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV). A suspension of 3.9 g. of powdered 2,2′-dinitro-6,6′-bis-(*m*-nitrophenyl)-diphenyl (XIII) in a solution of 26 g. of stannous chloride in 96 c.c. of glacial acetic acid which contains dry HCl was gently heated with occasional shaking until a clear solution resulted, dry HCl being passed in all the time. It was observed that, when the reaction mixture was heated at a higher temperature (over 70° or so), the product separated as a gelatinous mass which redissolved

when HCl was passed into the cooled mixture, showing that the solubility of the product decreases with the decrease of the HCl content in the reaction mixture. When the reaction was over, the solvent was removed by distillation in vacuum, and the residue dissolved in water, made alkaline, and the free base collected. It was purified by vacuum distillation and then by crystallization from EtOH, from which 2,2′-diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV) separated as almost colourless, large crystals which melted at 169–170° (Found: N. 15.43. Calc. for $C_{24}H_{22}N_4$: N, 15.30%). The yield of the pure crystals was 2.5 g. The tetramino-compound, unlike most of the aromatic amines, is sparingly soluble in ether and benzene. It is moderately soluble in EtOH when hot and sparingly so in the cold.

Attempts to isolate the tetramine as its hydrochloride from the reaction mixture were also made, but besides some other reason which has not been made clear, as the hydrochloride is very soluble even in conc. HCl, the result was not satisfactory.

4,5-Bis-(*m*-aminophenyl)-carbazole (XV). A solution of 0.61 g. of 2,2′-diamino-6,6′-bis-(*m*-aminophenyl)-diphenyl (XIV) in 20 c.c. of 0.5 N HCl solution in the nitrogen atmosphere was heated in a sealed tube in an oil bath at 200–205° for 7 hours, and then left overnight in the cold. As it is difficultly soluble even in a greatly diluted HCl, the carbazole derivative (XV) separated almost completely as a gray powdery dihydrochloride, but a few c.c. of conc. HCl was added to complete its separation, the dihydrochloride was collected, washed with dil. HCl and dried in vacuum over soda lime. The product (0.69 g.) was the almost pure dihydrochloride of XV. The method of purification such as the redissolution of the dihydrochloride in water, followed by the addition of conc. HCl after being treated with animal charcoal did not remove a trace of the impurity present. The crude product was therefore dissolved in water, made alkaline, and the base thus set free extracted with ether, when a trace of the dark impurity remained undissolved. The ethereal solution thus obtained was still somewhat coloured, but on leaving overnight with the addition of anhydrous K_2CO_3 or KOH, it became almost colourless. The ether was then removed at as low a temperature as possible to avoid oxidation of the base which tends to darken in colour at higher temperatures. The gummy residue was subsequently dried in high vacuum. It weighed 0.57 g. All attempts to purify the base by crystallization from a solvent and from mixed solvents failed, but on rubbing this gum with a small quantity of EtOH, a small portion of it was obtained as a solid form, which melted fairly sharply at 180–182° after softening at 175°.

The free base is readily soluble in ether, benzene, MeOH, and EtOH, and insoluble in petroleum ether. The solutions had a violet fluorescence, as was also observed in solutions of its salts and the acyl derivatives prepared so far. As stated above, the base, when heated at higher temperatures, darkens in colour and passes into a substance or substances insoluble or difficultly soluble in ether and benzene.

To obtain the pure dihydrochloride, the gummy base obtained above was dissolved in the calculated quantity of dil. HCl, and the dihydrochloride precipitated by the addition of a few c.c. of conc. HCl. It was collected and dried in vacuum over soda lime at ordinary temperature. It formed nearly colourless powdery crystals containing two molecules of water of crystallization (0.1858 g. of the dihydrochloride lost 0.0136 g. at 100° and 7 mm. pressure. Found: H_2O, 7.32; N, 9.42; Cl, 15.28. Calc. for $C_{24}H_{19}N_3 \cdot 2HCl \cdot 2H_2O$: H_2O, 7.86; N, 9.17; Cl, 15.48%). Aqueous solutions of the dihydrochloride darkened gradually when left in the air. This rather easily oxidisable nature was also

observed in solutions of the other salts of this base. Apparently, in solutions, these salts were oxidized more readily than the free base.

As already stated in the introduction, attempts to resolve this base with *d*-camphor sulphonic acid and *d*-tartaric acid have not been successful. No crystalline substance was formed when a conc. solution of this base in EtOH or in a mixture of EtOH and benzene was treated with *d*-camphor sulphonic acid. With *d*-tartaric acid, the base formed a difficultly soluble salt or salts in EtOH, but the deep brown colour of this salt rendered polarimetric examination impossible. Furthermore, as the material available for the investigation was very small, it was not possible to make a detailed examination of these salts.

4,5-Bis-(*m*-acetamidophenyl)-carbazole. The gummy 4,5-bis-(*m*-aminophenyl)-carbazole (XV) (0.20 g.) was dissolved in 12 c.c. of benzene and treated with an excess of acetic anhydride. The very difficultly soluble diacetyl derivative separated at once as an amorphous mass, which slowly but completely crystallized when the mixture was heated under reflux. After two hours' heating almost colourless crystals (0.21 g.) melting at 257–258° were obtained (Found : N, 9.90. Calc. for $C_{28}H_{23}O_2N_3$: N, 9.70%). There was no indication of the existence of the two forms.

4,5-Bis-(*m*-*l*-menthoxyacetamidophenyl)-carbazole. To a mixture of 0.32 g. of anhydrous K_2CO_3 and a solution of 0.20 g. of 4,5-bis-(*m*-aminophenyl)-carbazole (XV) in 20 c.c. of benzene was added 0 40 g. of *l*-menthoxyacetylchloride prepared from *l*-menthoxyacetic acid[18] by the method of Holmes and Adams[19], and the mixture refluxed on the water bath for two hours. It was then shaken with water to remove the excess of *l*-menthoxyacetic acid, and the upper layer, after being dried with Na_2CO_3, evaporated up. The residual syrup, on being left in a basin, partly crystallized, but as the residual mass was not easily brought into crystallization it was rubbed with 12 c.c. of ether, and the crystals thus obtained were collected and washed. The colourless powder thus obtained weighed 0.19 g. It was dissolved in 10 c.c. of boiling EtOH, and the solution evaporated until the bulk was 6 c.c. and left overnight. In this way, all the dissolved substance (0.19 g.) slowly separated in almost colourless, well-defined crystals melting at 190–191° (Found : N, 5.77. Calc. for $C_{48}H_{59}O_4N_3$: N, 5.67%). Rotation : 0.0741 g. made up to 15 c.c. with benzene gave α_D +0.14° ($l = 2$), $[\alpha]_D$ +14.2°, 0.0741 g. made up to 15 c.c. with EtOH gave α_D −0.22° ($l = 2$), $[\alpha]_D$ −22.27°, 0.0852 g. made up to 15 c.c. with acetone gave α_D −0.28° ($l = 2$), $[\alpha]_D$ −24.65°.

The ethereal mother liquor and the washings obtained above were evaporated up and the residue twice crystallized from a few c.c. each of EtOH. The crystals thus obtained (0.12 g.), though had somewhat lower melting point (188° after sintering at 185°) than the main crop, showed no depression of the melting point when they were mixed together, and possessed the same crystalline form and the same rotation as the main crop, showing that they were one and the same substance. The total yield of the *l*-menthoxyacetyl compound was therefore 0.31 g. or 73% of the theoretical.

The *l*-menthoxyacetyl compound was hydrolysed with great difficulty. Thus, in one instance, when 0.14 g. of the diacyl compound was refluxed with a mixture of 5 c.c. of conc. HCl and 7 c.c. of EtOH for 14 hours, 0.06 g. of the original substance was recovered unchanged. In addition, there was also deposited from the reaction mixture 0.04 g. of

(18) Frankland and O'sullivan, *J. Chem. Soc.*, **99** (1911), 2329.
(19) Holmes and Adams, *J. Am. Chem. Soc.*, **56** (1934), 2093.

a crystalline hydrochloride which was quite stable in the air. The free base could be precipitated by adding alkali to its solution in water. This hydrochloride had $\alpha_D = 0$ in water, and so was the rotation of the free base in benzene. From these properties it is inferred that this hydrochloride might have been a product obtained by the removal of one of the menthoxyacetyl groups and also of the menthoxyl group of the other menthoxyacetamido-group. The analysis of the nitrogen content in the hydrochloride showed that the figure found agreed fairly well with that calculated for the monoglycolyl derivative of XV containing one molecule of water of crystallization. The conclusive proof of the structure of this substance could not be obtained on account of lack of material.

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SYNTHETISCHE VERSUCHE IN DER SELENOPHENGRUPPE. I. EINWIRKUNG VON CHLOR UND BROM AUF SELENOPHEN.

Von **Harusada SUGINOME** und **Sumio UMEZAWA.**

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Das Selenophen (I), das dem Thiophen entsprechende Selenderivat, ist von Foa[1] aus bernsteinsaurem Natrium durch Erhitzen mit Phosphortriselenid in schlechter Ausbeute als ein Öl, Sdp. 147–149°/250 mm., erhalten worden. Nach ihm haben Bogert und Andersen[2] durch Erhitzen von Bernsteinsäure mit Phosphorpentaselenid ein Öl erhalten, das dem von Foa beschriebenen Selenophen sehr ähnlich war. Kürzlich veröffentlichten Briscoe und seine Mitarbeiter[3] eine schöne Darstellungsmethode von Selenophen aus Acetylen und Selen bei ca. 400°. Selenophen wird als schweres gelbes Öl, Sdp. 109.9–110.1°/752.1 mm., mit nicht angenehmem, an Benzol und Schwefelkohlenstoff erinnerndem Geruch erhalten.

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(1) *Chem. Zentr.*, **81** (1910), I, 837; *Gazz. chim. ital.*, **39** (1909), II, 527.

(2) *J. Am. Chem. Soc.*, **48** (1926), 225.

(3) H. V. A. Briscoe und J. B. Peel, *J. Chem. Soc.*, **1928**, 1741. H. V. A. Briscoe und P. L. Robinson, *ibid.*, **1928**, 2628. McMahon, T. G. Pearson und P. L. Robinson, *ibid.*, **1933**, 1644.

Die Einwirkung von Acetylen auf Selen wurde auch von Mazza und Solazzo[4] untersucht. Sie liessen reines Acetylen auf Selen bei 250-300° einwirken und isolierten durch fraktionierte Destillation ein bei 113-114° siedendes Öl, Selenophen. Die Angaben über das Selenophen in der Literatur[5] sind also sehr verschieden, und es scheint uns, als ob noch nicht viele seiner Derivate synthetisch hergestellt worden seien. Da in unserem Land verhältnismässig reichlich Selen produziert wird—die Sumitomo-Bessiberg-Aktiengesellschaft stellte uns freundlicherweise eine ziemlich grosse Menge von Selendioxyd und Kammerschwamm zur Verfügung, wofür wir nochmals an dieser Stelle unseren Dank aussprechen möchten—so haben wir die vorliegende Arbeit unternommen.

Auch wir liessen Acetylen auf Selen in einem Porzellanrohr bei 350-370° einwirken. Die Resultate haben die Beschreibung von Briscoe und seinen Mitarbeitern[3] bestätigt und zwar fanden wir, dass die Ausbeute, wenn man die Reaktion unter bestimmten Bedingungen ausführt, etwa 35% der Theorie erreichen kann.

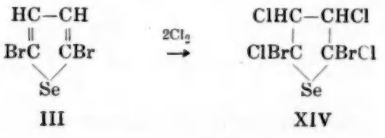
Führt man bei tiefer Temperatur wasserfreies Chlor in das mit Schwefelkohlenstoff verdünnte Selenophen ein, so tritt Selenophen-2, 3, 4, 5-tetrachlorid (VI), ohne Chlorwasserstoffentwicklung, als einheitlich gelbe Krystalle auf. Lässt man dasselbe sich thermisch zersetzen, so bildet sich das 2, 5-Dichlorselenophen (III) welches mit demjenigen identisch ist, das durch direkte Einwirkung von Chlor auf Selenophen erhalten wurde. Bei der thermischen Behandlung verwandelt sich das Tetrachlorid (VI) in einen sehr beständigen Isomer, 2, 2, 5, 5-Tetrachlortetrahydroselenophen (VIII).

Wenn man bei Zimmertemperatur dieselbe Lösung mit einer berechneten Menge Chlor behandelt, so entstehen unter Chlorwasserstoffentwicklung 2-Chlorselenophen (II), 2, 5-Dichlorselenophen (III) und Selenophentetrachlorid (VI), während sich mit überschüssigem Chlor 2, 5-Dichlorselenophen-2, 3, 4, 5-tetrachlorid $C_4H_2Cl_6Se$ (X) neben den oben erwähnten drei Chlorderivaten (II, III, VI) bildet. Die Hexachlorverbindung wurde auch aus 2, 5-Dichlorselenophen (III) durch vorsichtige Behandlung mit Chlor gewonnen. Lässt man aber bei 50-60° Chlor auf Selenophen ohne Lösungsmittel einwirken, treten keine gelben Krystalle auf, sondern Monochlor- (II), Dichlor-selenophen (III) und Dichlorselenophentetrachlorid (X) sind dargestellt. Die Bildung von einem solchen Dihalogenselenophentetrachlorid wurde beim Behandeln des 2, 5-Dibromselenophen (III) mit Chlor bestätigt und dabei erhielten wir das dem

(4) *Chem. Zentr.*, **100** (1929), I, 1454; *Rend. accad. sci.* (*Napoli*), Serie 3a, **33** (1927), 236.

(5) Die Konstanten des Selenophens von Foa sind von Richter-Anschütz, „Chemie der Kohlenstoffverbindungen" (12 Auflage, 1931, Bd. III) angenommen worden.

Dichlorselenophentetrachlorid (X) ähnliche 2, 5-Dibromselenophen-2, 3, 4, 5-tetrachlorid (XIV).

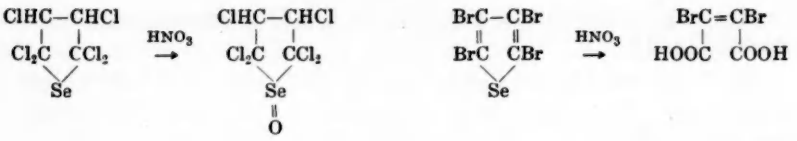


III XIV

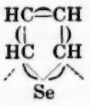
Die Einwirkung von Brom auf Selenophen wurde wie beim Chlor untersucht und gewannen wir dabei Substitutions- wie auch Additions-produkte. Unter diesen Selenophenderivaten sind 2,3,5-Tribrom- (IV), Tetrabromselenophen (V), und 2,2,5,5-Tetrabromtetrahydroselenophen-1,1-dibromid (IX), welche beim Chlor nicht erhalten wurden. Beim Behandeln des Selenophens mit überschüssigem Brom bei tiefer Temperatur konnten wir Selenophen-2,3,4,5-tetrabromid und Hexabromverbindung, welche beim Chlor erhalten wurden, nicht gewinnen. Das oben beschriebene Dibromid (IX), färbt sich gelblich, wird mit Wasser, besonders mit wässerigem Alkali zersetzt, indem die Bromatome am Selen sich spalten, wobei das farblose 2,2,5,5-Tetrabromtetrahydroselenophen (VIII) gebildet wurde. Unter den mit Wasser zersetzten Produkten konnten wir auch ein Selenoxyd $C_4H_4Br_4SeO$ (XI) isolieren, das durch Oxydation des Tetrabromtetrahydroselenophen (VIII) mit rauchender Salpetersäure gewonnen wurde. Neuerdings haben Morgan und Burstall[6] von einem mit dem oben beschriebenen Selenoxyd (XI) nahe verwandten Tetrahydroselenophen-1,1-dihydroxyd (XIII) Mitteilung gemacht. Diese Verfasser haben das interessante Dihydroxyd durch Behandlung des Tetrahydroselenophen-1,1-dibromids mit Silberoxyd dargestellt. Es scheint uns nicht ohne Interesse, dass das Dihydroxyd des halogenierten Tetrahydroselenophens unbeständig ist und Wasser abspaltet. Wir haben noch einen Beweis für die Bildung eines solchen Selenoxyd gefunden. Beim Kochen des Selenoxyds mit Cyclohexanol entsteht nämlich das Tetrabromtetrahydroselenophen (VIII). Das letztere wurde durch Anlagerung des Broms an Selenatom ins Dibromid (IX) eingeführt, welches beim Kochen mit Toluol umkehrbar ist.

Was die Orientierungen der Halogene in den oben beschriebenen Selenophenderivaten betrifft, so können wir schliessen, dass, wie beim Thiophen oder Furan, α-ständige Wasserstoffatome leichter als β-ständige angegriffen werden. Zum Zweck des direkten Beweises für die Orientierungen der Halogene oxydierten wir natürlich die oben erhaltenen Derivate mit rauchender Salpetersäure. Dabei fanden wir, dass die Tetrahydroselenophenringe ausserordentlich widerstandsfähig gegen das Oxydationsmittel sind und Selenoxyden als Oxydationsprodukt liefern. Die halogensubstituierten Selenophenringe sind im Gegenteil gegen Salpetersäure unbeständig und geben halogenierte Maleinsäure. Zum Beispiel:

(6) *J. Chem. Soc.*, **1929**, 1096.



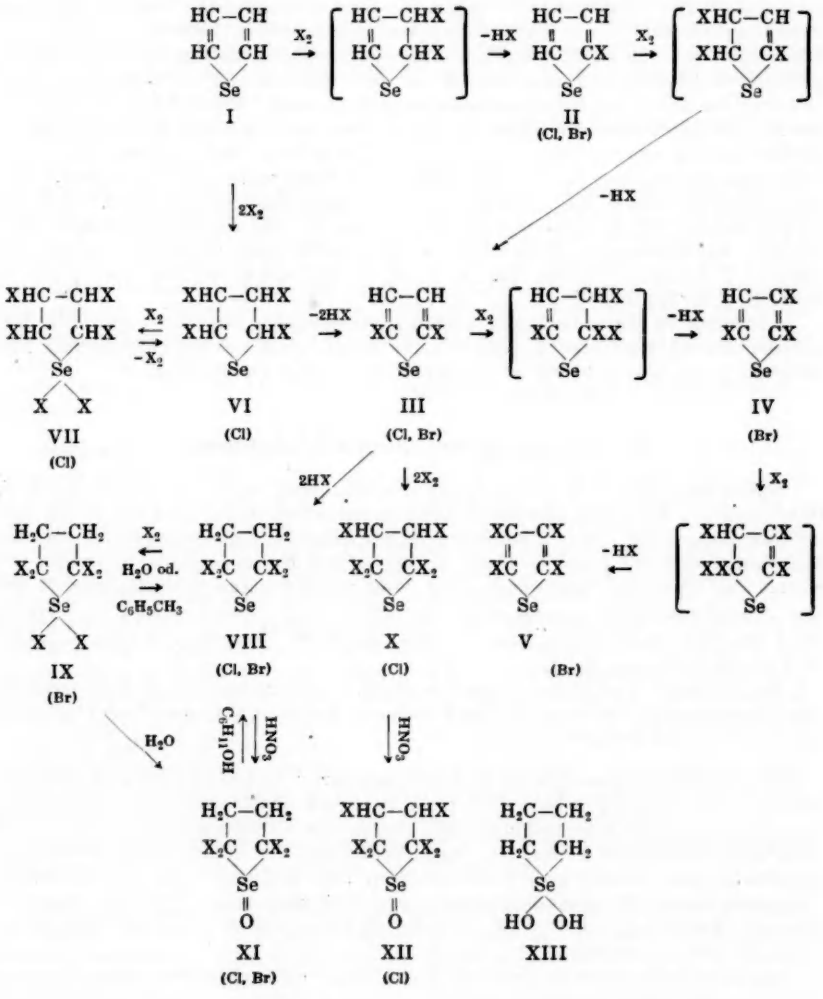
Vor kurzem haben Gilman und Wright[7] berichtet, dass das Furan ein dynamisches Gleichgewicht von mehreren Strukturformeln zu sein scheint. Hinsberg[8] hat über die Thiophenformel eine aufgestellt, die freie Valenzkräfte am Schwefel annimmt. Danach stellte Steinkopf[9], der sich eingehend mit der Thiophengruppe beschäftigt hat, durch Anwendung der Partialvalenzentheorie eine vortreffliche Thiophenformel auf. Wir können infolgedessen die Steinkopfsche Formel ohne weiteres auf das Selenophen anwenden, womit man die Einwirkungen der Halogene auf das Selenophen genügend erklären kann. Der Grund des ungesättigten Charakters des Selenophens beruht wahrscheinlich darauf, dass die inaktive Doppelbindung zwischen C und Se offenbar einen geringeren Grad Festigkeit besitzt als die zwischen C und C, und dass, infolge der kleineren Partialvalenzen am Se diese nicht genügen, die der benachbarten C-atome völlig abzusättigen, so dass an letzteren geringe Affinitätsbeträge übrig bleiben und sich das Bild der nebenstehenden Formel ergibt.



Bemerkenswert ist, dass Selenophen sich viel weniger aromatisch als Thiophen verhält, indem das erstere bei Einwirkung von Halogenen die Additionsprodukte leicht ergibt. Diese verlieren freiwillig oder leicht durch die thermische Behandlung Halogenwasserstoffe und so entstehen die Substitutionsprodukte. Bei den Olefinen aber bleiben die Reaktionen meist bei der ersten Phase der Addition stehen. Was die Mechanismen der Substitution von Thiophenen oder Benzolen betrifft, so könnten sie wie beim Selenophen erklärt werden, die Anlagerung an die Doppelbindungen tritt nämlich als primärer Vorgang auf und es entstehen durch nachfolgende Abspaltung substituierte Substanzen. Diesen Schluss haben schon Steinkopf[9], Wieland und Bettag[10] aus ihren Beobachtungen gezogen. Sie scheinen sie aber noch nicht an Thiophenen oder an Benzolen experimentell nachgewiesen zu haben. Doch scheint sich die Reihenfolge: Olefine, Selenophene, Thiophene, Benzole, und Furane zu ergeben.

(7) *Chem. Rev.*, **11** (1932), 323.
(8) *J. prak. Chem.*, (2), **93** (1916), 302.
(9) *Ann.*, **430** (1923), 94.
(10) *Ber.*, **55** (1922), 2246.

Die folgende Übersicht erklärt wohl die Einwirkungsmechanismen der Halogene auf Selenophen.



Beschreibung der Versuche.

Zur Darstellung des Selenophens. Im wesentlichen wurde nach den Angaben von Briscoe und seinen Mitarbeitern[3] gearbeitet. Gereinigtes Acetylen liess man auf 20 g. Selen bei 350–370° einwirken, welches sich in einem Porzellanschiffe innerhalb eines Porzellanrohres befand. Nach der Reaktion war eine schwarze, teerartige Substanz im Schiffe geblieben. Dieser Rückstand, wie Briscoe und seine Mitarbeiter schon bemerkten, wirkt als Katalysator und zwar fanden wir, dass die Ausbeute von Selenophen durch Mischung des Selens mit dem Katalysator ziemlich zunimmt. Ferner hängt die Ausbeute von der Geschwindigkeit des Gases ab; deshalb muss man die Reaktion in ungefähr 24 Stunden zu Ende kommen lassen. Bei der Ausführung kann man die gleiche Menge dunkelbraunes Öls (Sp. Gew. = 1.47) mit derselben des angewandten Selens erhalten. Man fraktioniert das rohe Öl mittelst eines Ladenburgschen Kölbchens zweimal, wobei der Hauptanteil bei 110° überging und aus 192 g. rohem Öl 110 g. reines Selenophen erhalten wurden. Die Ausbeute des Selenophens beträgt 57% der rohen Flüssigkeit und 35% des Selens. $d_4^{15°}$ 1.5301; $n_D^{15°}$ 1.568. Gef.: C, 36.33; H, 3.14; Se, 60.01. Ber. für C_4H_4Se: C, 36.60; H, 3.08; Se, 60.36%.

Selenophen ist beständig gegen konzentrierte Salzsäure wie auch gegen Alkalien, reagiert aber auf konzentrierte Schwefelsäure sofort, wobei sich ein dunkelgrüner Niederschlag bildet, ebenso heftig ist die Reaktion auf konz. Salpetersäure.

I. Einwirkung von Chlor auf Selenophen.

2-Chlorselenophen (II). In 4 g. erwärmtes Selenophen werden 2 g. Chlor langsam bei 50–60° geleitet, wobei sich sehr heftig Chlorwasserstoff entwickelt und die Lösung dunkelbraun gefärbt ist. Nach 2 stündigem Stehenlassen bei Zimmertemperatur wird das Reaktionsgemisch mit Äther verdünnt, mit verdünntem Natriumcarbonat gewaschen und zuletzt über Glaubersalz getrocknet. Das Lösungsmittel wurde dann eingedampft und der Vakuumdestillation unterworfen. Sdp. 42°/12.5 mm. Ausbeute 3.5 g., $d_4^{14°}$ 1.6621; $n_D^{20°}$ 1.594. Gef.: C, 28.68; H, 2.14; Cl, 20.94; Se, 47.46. Ber. für C_4H_3ClSe: C, 28.97; H, 1.83; Cl, 21.36; Se, 47.71%.

Bei der Reaktion erhält man höher siedendes 2, 5 Dichlorselenophen als Nebenprodukt. Das Chlorselenophen bildet eine farblose Flüssigkeit, hat dem Chlorbenzol ähnlichen Geruch und zeigt deutlich Indopheninreaktion.

2,5-Dichlorselenophen (III). Zu 4g. Selenophen werden 4g. Chlor langsam bei 50–60° eingeleitet. Nach 2 stündigem Stehenlassen bei Zimmertemperatur wird das hierbei erhaltene dunkelbraune Öl mit Äther verdünnt, mit verdünntem Natriumcarbonat gewaschen und dann über Chlorcalcium getrocknet. Nach Verdunsten des Äthers wurde im Vakuum destilliert, wobei vorläufig geht Chlorselenophen über und dann wird das 2,5-Dichlorselenophen als der Hauptanteil erhalten. Sdp. 67°/12 mm. oder 71°/18 mm. Ausbeute 3.0 g. $d_4^{14°}$ 1.8372; $n_D^{14°}$ 1.606. Gef.: C, 23.83; H, 1.33; Cl, 35.48. Ber. für $C_4H_2Cl_2Se$: C, 23.95; H, 1.06; Cl, 35.38%.

Das Dichlorselenophen ist fast farblos und stark lichtbrechend, hat einen charakteristischen Geruch und zeigt Indopheninreaktion beim Erwärmen. Die bei der Fraktionierung im Kolben zurückbleibenden Anteile scheiden beim Erkalten im Eisschranke eine kleine Menge von farblosen Krystallen aus. Nach Umkrystallisation wurde sie als 2, 5-Dichlorselenophen-2, 3, 4, 5-tetrachlorid (X) identifiziert.

2, 5-Dichlorselenophen-2, 3, 4, 5-tetrachlorid (X). In ein Reagenzglas bringt man 3 g. Selenophen, erwärmt es auf 60° und leitet dann überschüssiges Chlor langsam ein, wobei sich eine etwas zähige Flüssigkeit bildet. Nach 2 stündigem Stehenlassen bei Raumtemperatur wurde sie wie oben beschrieben aufgearbeitet. Das braungefärbte, dickflüssige Öl wird im Vakuum destilliert, wobei sich eine kleine Menge noch flüssiger Anteile abdestilliert und der Rückstand beim Erkalten krystallin erstarrt. Ausbeute 3.0 g. Dieser wird aus Alkohol dreimal umkrystallisiert, wobei sich die Substanz in Rosetten ausscheidet. Schmp. 55°. Gef.: C, 14.44, 14.13; H, 0.88, 0.85; Cl, 62.09. Ber. für $C_4H_2Cl_6Se$: C, 14.04; H, 0.59; Cl, 62.21%.

Die Substanz ist leicht löslich in Äther, Benzol, Chloroform, Petroläther und Schwefelkohlenstoff, aber unlöslich in Wasser.

Oxydation von Dichlorselenophen-2, 3, 4, 5-tetrachlorid (X) **mit rauchender Salpetersäure.** In auf −21° abgekühlte, rauchende Salpetersäure versetzt man 0.1 g. Dichlorselenophen-2, 3, 4, 5-tetrachlorid und lässt die Temperatur des Reaktionsgemisches allmählich auf +15° steigen. Verdünnt man die dabei gebildete, klare Lösung sofort mit ca. 50 c.c. kaltem Wasser, so scheidet sich ein farbloser krystallinischer Körper aus. Man saugt diesen ab und wäscht ihn mit Alkohol und Äther. Ausbeute 0.1 g. Umkrystallisiert aus Ligroin. Feine Nadeln. Schmp. 172-172.5° unter heftigem Aufschäumen. Gef.: Cl, 59.33. Ber. für $C_4H_2Cl_6SeO$: Cl, 59.43%.

Das Oxyd ist löslich in Alkohol, Äther, Ligroin und Benzol, aber schwerlöslich in Petroläther.

Selenophen-2, 3, 4, 5-tetrachlorid (VI). Man löst 3 g. Selenophen in 12 c.c. Schwefelkohlenstoff und leitet dazu 4 g. Chlor langsam bei −15° ein. Es entstehen sofort gelbe, tafelförmige Krystalle, während sich der Chlorwasserstoff noch nicht entwickelt. Es ist deutlich, dass diese Krystalle, ein Chloranlagerungsprodukt, Selenophen-2, 3, 4, 5-tetrachlorid-1, 1-dichlorid (VII) sind. Dieses Chlorderivat ist aber so unbeständig, dass sich beim Absaugen explosivartig Chlor entwickelt und sich in Selenophen-2, 3, 4, 5-tetrachlorid (VI) verändert. Beim Stehenlassen des Reaktionsgemisches bei -15° entfärbt es sich, indem die ausgeschiedenen gelben Krystalle Chloratome am Selen abspalten. Das dabei entstandene, farblose Tetrachlorid wird schnell abgesaugt und mit Schwefelkohlenstoff gründlich gewaschen. Ausbeute 2 g. Es schmilzt bei 97° unter Aufschäumen und Bräunung. Es ist in gewöhnlichen Lösungsmitteln unlöslich. Das Tetrachlorid ist ohne Zersetzung nicht umkrystallisierbar. Gef.: C, 17.66, 17.77; H, 1.64, 1.54; Cl, 52.27. Ber. für $C_4H_4Cl_4Se$: C, 17.58; H, 1.48; Cl, 52.00%.

Briscoe und Peel[11] haben auch eine Tetrachlorverbindung nach denselben Bedingungen erhalten und sie nahmen an, dass diese Chlorverbindung statt des Anlagerungsprodukts ein Substitutionsprodukt, nämlich Tetrachlorselenophen, wäre.

Ferner untersuchten wir sein Verhalten gegen rauchende Salpetersäure bei tiefer Temperatur und erhielten Oxalsäure als Oxydationsprodukt.

Thermische Zersetzung von Selenophentetrachlorid (VI). Man lässt 4 g. Selenophentetrachlorid bei 95° im Paraffinbade allmählich sich zersetzen, wobei sich heftig Chlorwasserstoff entwickelt. Nach Vollendung der Zersetzung verdünnt man die dabei gebildete, dunkelbraune Flüssigkeit mit Äther, behandelt sie mit Natriumcarbonatlösung und arbeitet sie auf. Das entstandene Öl wurde im Vakuum fraktioniert. Dichlorselenophen (III) destilliert sich bei 70.8° unter 15 mm. Ausbeute 1 g. In jeder Hinsicht ist diese

(11) *J. Chem. Soc.*, **1928**, 1741.

farblose, stark lichtbrechende Flüssigkeit identisch mit dem oben beschriebenen 2,5-Dichlorselenophen (III). $n_D^{15°}$ 1.606. Gef.: Cl, 35.65. Ber. für $C_4H_2Cl_2Se$: Cl, 35.38%.

Der bei dieser Fraktionierung gebliebene Rückstand scheidet im Eisschranke prachtvolle, farblose Krystalle aus, welche abgesaugt und aus Alkohol umkrystallisiert werden. Schmp. 96–98°. Gef.: C, 17.34, 17.16; H, 1.83, 1.83; Cl, 52.17. Ber. für $C_4H_4Cl_2Se$: C, 17.58; H, 1.48; Cl, 52.00%.

Die Tetrachlorverbindung, 2,2,5,5-Tetrachlortetrahydroselenophen (VIII), ist leicht löslich in Lösungsmitteln und weitaus beständiger als das andere, welches sich bei 97° zersetzt.

Diese Tetrachlorverbindung wurde mit rauchender Salpetersäure oxydiert und ein Selenoxyd erhalten. Man versetzt 0.15 g. 2,2,5,5-Tetrachlortetrahydroselenophen in –18° abgekühltem 2 c.c. rauch. Salpetersäure. Nach einigen Minuten verdünnt man diese klare Lösung mit 50 c.c. kaltem Wasser. Es scheidet sich nach einiger Zeit ein farbloser, krystallinischer Körper aus, welcher in organischen Lösungsmitteln schwer löslich ist. Ausbeute 0.05 g. Schmp. 149–150° unter heftigem Aufschäumen. Gef.: Cl, 49.33. Ber. für $C_4H_4Cl_4SeO$: Cl, 49.11%.

II. Einwirkung von Brom auf Selenophen.

2,2,5,5-Tetrabromtetrahydroselenophen-1,1-dibromid (IX). Man verdünnt 2 g. Selenophen mit 5 c.c. Schwefelkohlenstoff und lässt dann unter Schütteln im Kältegemisch bei ca. –15° aus dem Tropftrichter nach und nach eine 20%-ige Lösung von Brom darein eintropfen. Unter gelinder Bromwasserstoffentwicklung scheidet es bei der Reaktion gelbe Krystalle aus. Ist die ganze Bromlösung versetzt, so werden die gelben Krystalle sofort abgezogen und mit Schwefelkohlenstoff genügend gewaschen. Ausbeute 1 g. An der Luft zersetzt sich dieses Präparat allmählich und ist unbeständig gegen Wasser, besonders gegen wässerige Säuren und Alkalien, die dasselbe zu dem unten erwähnten, farblosen Körper sich entfärben lassen. Nach der Umkrystallisierung aus wasserfreiem Benzol schmilzt es bei 152° unter Aufschäumen und Bräunung. Gef.: C, 7.98, 8.03, 8.05; H, 1.09, 0.99, 1.01; Br, 78.10, 78.02, 78.20; Se, 12.54, 12.42, 12.48. Ber. für $C_4H_4Br_6Se$: C, 7.86; H, 0.66; Br, 78.26; Se, 12.97%.

Die Hexabromverbindung ist in gewöhnlichen Lösungsmitteln schwer löslich und zeigt keine Indopheninreaktion in der Kälte, nur eine undeutliche beim Erhitzen.

Die Brom-ionen und -moleküle, welche aus Tetrabromtetrahydroselenophen-1,1-dibromid (IX) beim Behandeln mit Wasser abgespalten wurden, wurden auf folgende Weise titriert. Das pulversierte Dibromid 0.3907 g. wurde mit ca. 5 c.c. Wasser versetzt und mit Äther umgeschüttelt. Die Ätherschicht wurde dreimal mit Wasser gewaschen, das gesamte Wasser mit 1 g. Kaliumjodid, das in einer kleinen Menge von Wasser gelöst ist, versetzt, wobei die Jodmoleküle, welche den freien Brommolekülen entsprechen, sich befreien. Sie wurden mit Natriumthiosulfatlösung mittels Indikators von einigen Tröpfchen der Stärkelösung titriert (a). Dann wurde das Reaktionsgemisch noch einmal mit 1 g. Kaliumjodat, das in einer kleiner Menge von Wasser gelöst ist, versetzt und bis zur Entfärbung mit Natriumthiosulfat titriert (b).

Das gesamte Natriumthiosulfat (b) zeigt das gesamte Brom, welches aus dem Dibromid sich spaltet und die Differenz ($b-a$) entspricht den Bromionen, welche durch Hydrolyse als Bromwasserstoff aus dem Dibromid sich abspalten. Natriumthiosulfatlösung: 0.1004 N. Brom als Brommoleküle = a = 0.82 c.c. = 0.0104 g. Jod = 0.0066 g. Brom = 1.68% des Di-

bromids. $b = 12.55$ c.c. Brom als Bromionen $= b-a = 11.73$ c.c. $= 0.1494$ g. Jod $= 0.0941$ g. Brom $= 24.09\%$ des Dibromids. Gef.: Gesamtes Br, 25.77% des Dibromids. Ber. für $Br_2/C_4H_4Br_6Se$: Br, 26.17%.

2, 2, 5, 5-Tetrabromtetrahydroselenophen (VIII). Versetzt man 3 g. gelbe Hexabromverbindung (IX) mit überschüssigem kaltem Wasser und schüttelt es, so entfärbt sich dies allmählich. Nach vollständiger Entfärbung wird das Reaktionsgemisch mit Äther wieder umgeschüttelt, wobei ein Anteil des farblosen Körpers in die Oberschicht geht, während der Rest noch unlöslich vorhanden ist. Man trennt die Ätherschicht und trocknet sie über Chlorcalcium. Verdampft man das Lösungsmittel im Vakuum bei Zimmertemperatur, bleibt ein farbloses, krystallinisches Produkt zurück, welches in Lösungsmitteln leicht löslich ist. Ausbeute 0.2 g. Aus Alkohol umkrystallisiert. Tafelförmige Krystalle. Schmp. 97° (ohne Zersetzung). Gef.: C, 10.59, 10.66; H, 1.15, 1.08; Br, 70.83, 70.79; Se, 17.43. Ber. für $C_4H_4Br_4Se$: C, 10.64; H, 0.89; Br, 70.85; Se, 17.56%.

Bei langer Aufbewahrung zersetzt sich dies allmählich von selbst unter Färbung.

Man kann das Tetrabromtetrahydroselenophen-1,1-dibromid (IX) aus Tetrabromtetrahydroselenophen (VIII) auf folgende Weise durch Bromanlagerung wiedererzeugen. Man löst 0.1 g. Tetrabromtetrahydroselenophen in 2 c.c. Schwefelkohlenstoff, versetzt es mit 0.5 c.c. Brom und bewahrt die klare Lösung 2 Tage lang bei Raumtemperatur unter Ausschluss von Feuchtigkeit auf. An der Wand des Gefässes scheiden sich prachtvolle gelbe, tafelförmige Krystalle ab, welche abgesaugt und mit Schwefelkohlenstoff gewaschen werden. Umkrystallisiert aus wasserfreiem Benzol; winzige gelbe Krystalle. Schmp. 152° unter Aufschäumen und Bräunung. Gef.: Br, 78.15; 78.27. Ber. für $C_4H_4Br_6Se$: Br, 78.26%.

2,2,5,5-Tetrabromtetrahydroselenophen-1-oxyd (XI). Der bei der Behandlung des Hexabromderivats (IX) mit Wasser entstandene, ätherunlösliche, farblose Anteil wurde abgesaugt und mit Alkohol und Äther gewaschen. Er sintert oberhalb 120° und zersetzt sich bei 123°. Unlöslich in Alkohol, Aceton, Essigester, Benzol, Chloroform, Petroläther, Schwefelkohlenstoff und Kohlenstofftetrachlorid und schwer löslich in Äther, Toluol und Eisessig. Wir probierten die Umkrystallisation aus Toluol erfolglos, weil es zersetzt. Zur Reindarstellung sättigten wir 85 c.c. Eisessig mit 0.1 g. dieser Substanz bei ca. 60° und nach der Abkühlung versetzten mit 30 c.c. Äther. Nach einiger Zeit im Eisschranke scheiden es sich allmählich winzige, farblose Krystallchen aus. Schmp. 128.5–130° unter Aufschäumung. Gef.: C, 10.51, 10.53; H, 1.27, 1.23; Br, 68.69. Ber. für $C_4H_4Br_4SeO$: C, 10.29; H, 0.86; Br, 68.47%.

Dieser Körper ist sehr beständig gegen chemische Reagenzien, sogar gegen erwärmte rauchende Salpetersäure. Dieses Selenoxyd wurde auch durch Oxydation des oben beschriebenen Tetrabromtetrahydroselenophens (VIII) mit rauchender Salpetersäure erhalten.

Oxydation von Tetrabromtetrahydroselenophen zu seinem Oxyd. In der auf –17° abgekühlten 1 c.c. rauchenden Salptersäure wird 0.1 g. Tetrabromtetrahydroselenophen gelöst. Man lässt die Temperatur des Reaktionsgemisches auf Zimmertemperatur steigen und verdünnt das Gemisch sofort mit 50 c.c. abgekühltem Wasser, wobei sich ein farbloser krystallinischer Körper ausscheidet. Dies wurde abgesaugt und mit Alkohol und Äther gewaschen. Das noch nicht umkrystallisierte Präparat zersetzt sich bei 124° unter Aufschäumen. Ausbeute 0.09 g. Umkrystallisiert aus Eisessig und Äther wie oben. Schmp. 129° unter Aufschäumen. Mischschmelzpunkt mit dem Präparat, das aus Tetrabrom-

tetrahydroselenophen-1,1-dibromid abgeleitet wurde, zeigt keine Depression. Gef.: C, 10.46; H, 1.05; Br, 68.08. Ber. für $C_4H_4Br_4SeO$: C, 10.29; H, 0.86; Br, 68.47%.

Reduktion von Tetrabromtetrahydroselenophen-1-oxyd (XI) zum Tetrabromtetrahydroselenophen (VIII). Zu 2 c.c. Cyclohexanol wird 0.1 g. Selenoxyd (XI) versetzt, durch Erhitzen gelöst und die Lösung weiter noch einige Minuten erhitzt. Man bringt sie in einer Krystallisierschale und lässt sie im Vakuumexsiccator über Paraffin einige Tage lang stehen. Es scheiden sich sehr langsam prächtige, tafelförmige Krystalle aus, die aus Alkohol umkrystallisiert sind. Schmp. 96–97.5°. Mischschmelzpunkt mit authentischem Präparat zeigt keine Depression.

Behandlung von Tetrabromtetrahydroselenophen-1,1-dibromid (IX) mit kochendem Toluol. In 2 c.c. Toluol wird 0.1 g. Dibromid durch Erwärmen allmählich gelöst. In der ersten Zeit ist die Lösung braun gefärbt, aber in der Nähe des Siedepunktes entwickeln sich tränenerregendes, bromiertes Toluol und Bromwasserstoff, während die Lösung sich entfärbt. Nach Vollendung der Bromwasserstoffentwicklung wird sie im Vakuumexsiccator über Paraffin und Alkali eingedunstet. Es scheidet sich 0.08 g. Tetrabromtetrahydroselenophen ab, welches aus Alkohol umkrystallisiert. Schmp. 95–96°. Mischschmelzpunkt mit Tetrabromtetrahydroselenophen zeigt keine Depression.

2-Bromselenophen (II). Zu wassergekühlter 10%-iger Schwefelkohlenstofflösung von 4 g. Selenophen tropft man eine 10%-ige Schwefelkohlenstofflösung von 4.8 g. Brom unter Umschütteln ein. Nach 2 stündigem Stehenlassen wird das Reaktionsgemisch mit verdünntem Natriumcarbonat gewaschen und über Chlorcalcium getrocknet. Nach Verdunsten des Lösungsmittels erhält man ein braunes Öl. Ausbeute 7.5 g. Wir versuchten anfangs sie unter atmosphärischem Druck zu destillieren, aber dabei fand die Zersetzung statt. Bei der Vakuumdestillation ging ein fast farbloses Öl über. Sdp. 59°/13 mm. Ausbeute 3.0 g. $d_4^{20°}$ 2.1003; $n_D^{20°}$ 1.635. Gef.: C, 23.03, 22.77; H, 1.36, 1.72; Br, 37.22, 37.28; Se, 37.46. Ber. für C_4H_3BrSe: C, 22.85; H, 1.44; Br, 38.03; Se, 37.69%.

Das Bromselenophen mischt sich in jedem Verhältnisse mit gewöhnlichen Lösungsmitteln, hat einen dem Brombenzol ähnlichen Geruch und zeigt deutlich Indopheninreaktion.

2, 5-Dibromselenophen (III) und 2, 3, 5-Tribromselenophen (IV). Zu 4 g. Selenophen in 10 c.c. Schwefelkohlenstoff wurden aus einem Tropftrichter 20 g. Brom in 10 c.c. Schwefelkohlenstoff unter Abkühlung und fleissigem Umrühren gebracht. Man lässt das Gemisch über Nacht bei Zimmertemperatur stehen, und bearbeitet es wie in den anderen Fällen. Das dunkelbraune, dickflüssige Öl wird im Vakuum destilliert. Nachdem das oben erwähnte Bromselenophen ca. 2.7 g. ausdestilliert, wird an zweiter Stelle 2, 5-Dibromselenophen erhalten. Sdp. 42°/0.02 mm. Ausbeute 4.1 g. $d_4^{20°}$ 2.5005; $n_D^{20°}$ 1.667. Gef.: C, 16.15, 16.62; H, 0.88, 1.24; Br, 55.09. Ber. für $C_4H_2Br_2Se$: C, 16.61; H, 0.70; Br, 55.31%.

Destilliert man die höher siedenden Anteile weiter, so erhält man noch ein Öl, das unter 0.12 mm. bei 94° kocht, und bei Raumtemperatur krystallinisch erstarrt. Ausbeute 2.9 g. Aus Alkohol kamen farblose Nadeln. Schmp. 38°. Gef.: C, 13.46, 13.31; H, 0.63, 0.75; Br, 65.04. Ber. für C_4HBr_3Se: C, 13.04; H, 0.27; Br, 65.15%.

Das Dibromselenophen ist fast farblos und stark lichtbrechend, mischt sich in jedem Verhältnisse mit organischen Lösungsmitteln und zeigt beim Erhitzen Indopheninreaktion. Auch das Tribromselenophen ist leicht löslich in Lösungsmitteln, zeigt aber beim Erhitzen nur undeutlich Indopheninreaktion.

Tetrabromselenophen (V). Selenophen ist ohne Lösungsmittel mit überschüssigem Brom unter Umschütteln in kaltem Wasser nach und nach versetzt, wobei sich sehr heftig Bromwasserstoff entwickelt. Lässt man das Reaktionsgemisch über Nacht stehen, so scheidet es farblose Nadeln aus. Ausbeute ist fast quantitativ. Schmp. 102°. In jeder Hinsicht stimmte unser Präparat mit der Beschreibung von Briscoe und Peel[11] überein. Gef.: C, 10.84, 10.63; H, 0.16; 0.17; Br, 71.48; Se, 17.68. Ber. für C_4Br_4Se: C, 10.74; H, 0.00; Br, 71.49; Se, 17.72%.

Oxydation von Tetrabromselenophen mit rauchender Salpetersäure. Trägt man 1 g. Tetrabromselenophen in 7 c.c. auf −18° abgekühlter, rauchender Salpetersäure (1.52) ein, so sinkt das Pulver grösstenteils unverändert zu Boden. Lässt man die Temperatur des Reaktionsgemisches allmählich steigen, so findet eine vollständige Lösung unter Rotfärbung und Entwicklung von Bromdämpfen statt. Giesst man die Flüssigkeit langsam in abgekühltes Wasser, so bildet sich anfangs eine krystallinische Ausscheidung, welche jedoch alsbald verschwindet. Nach einigen Tagen äthert man aus und erhält Dibrommaleinsäure. Ausbeute 0.53 g. Schmp. 120–123°. Die Säure wurde durch Behandlung mit Acetylchlorid und Schwefelsäure in Anhydrid[12], Schmp. 116°, abgeleitet und identifiziert. Gef.: Br, 62.09. Ber. für $C_4Br_2O_3$: Br, 62.48%.

2, 5-Dibromselenophen-2, 3, 4, 5-tetrachlorid (XIV) Da Weitz[13] und Rosenberg[14] 2,5-Dibromthiophen mit überschüssigem Chlor behandelt und Tetrachlorthiophen erlangt hat, probierten wir das Verhalten des Dibromselenophens gegen überschüssiges Chlor und fanden, dass in unserem Falle nur Anlagerung statt Austausch stattfand. Im gleichen Volumen Schwefelkohlenstoff sind 2 g. Dibromselenophen gelöst und bei Raumtemperatur wird ein Überschuss von Chlor langsam hineingeleitet. Nachdem eine kleine Menge des dabei ausgeschiedenen, gelben, krystallinischen Nebenproduktes abfiltriert ist, wird das Filtrat mit Äther verdünnt und mit Natriumcarbonat behandelt. Nach der Aufarbeitung erhält man ein dickflüssiges braunes Öl. Ausbeute 2 g. Bei der Vakuumdestillation ging nur eine kleine Menge von Öl zwischen 100–105° über, obwohl die Ölbadtemperatur 170° erreichte. Lässt man den Rückstand stehen, so scheiden sich nadelförmige, farblose Krystalle aus, welche abgesaugt werden. Aus Alkohol umkrystallisiert, farblose Nadeln. Schmp. 70–72°. Gef.: C, 11.50, 11.36; H, 0.64, 0.62; Cl, 32.40, 33.14; Br, 37.40, 35.81; Se, 17.96. Ber. für $C_4H_2Cl_4Br_2Se$: C, 11.40; H, 0.47; Cl, 32.90; Br, 37.08; Se, 18.37%.

Diese Substanz ist leicht löslich in Lösungsmitteln, dem Dichlorselenophentetrachlorid (X) in mancher Hinsicht ähnlich und zeigt sogar beim Erhitzen keine Indopheninreaktion.

Für Unterstützung der Kaiserlichen Akademie sind wir ihr zu Dank verpflichtet.

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(12) O. Diels und M. Reinbeck, *Ber.*, **43** (1910), 1274.
(13) *Ber.*, **17** (1884), 795.
(14) *Ibid.*, **19** (1886), 650.

ON THE ALKALOIDS OF WHITE HELLEBORE. II. ISOLATION OF ALKALOIDS FROM THE SO-CALLED RESINOUS MATTERS.

By Kojiro SAITO and Harusada SUGINOME.

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In the previous communication[1], a method of isolating alkaloids from the roots of white hellebore was described, but no account was given of the resinous matters soluble in alcohol but insoluble in water nor in dilute acetic acid. The former authors also laid aside, and did not investigate, this part of alkaloids, considering it as resin[2], as resinous substances[3] or as "unlösliche Bestandteile"[4]. Our subsequent investigation of the so-called resinous matters has shown the presence of another series of alkaloids.

The resinous matters were treated with dilute acetic acid to remove the soluble part, which gave alkaloids similar to those described in Part I on basifying with ammonia. This operation of extraction was very tedious, so that it was repeated until the yield of the bases amounted to 0.5% of the starting material.

The brown powder, insoluble in dilute acetic acid, was then treated with ether continuously and some oily matters as well as phenolic substances were removed. The latter were proved to consist chiefly of a dihydric phenol. Unfruitful attempts were made by using various solvents to obtain a crystalline substance from the powder. On treatment with dilute alkali the brown powder was decomposed into bases freely soluble in dilute acetic acid, and acidic substances with angelic acid and an acid melting at 102°. These acids, however, were rather small in amount and the acidic substances were found to be phenolic acids sparingly soluble in ether. The crude bases thus obtained could be crystallised from dilute alcohol but isolation of the components in pure condition was unsuccessful. Then they were divided into seven fractions by fractional precipitation, as done in Part I. On neutralizing each fraction with hydrochloric acid in alcohol, the first three gave jervine hydrochloride in crystalline form. From the fourth fraction some more hydrochloride could be obtained.

(1) This Bulletin, **9** (1934), 15.

(2) Wright and Luff, *J. Chem. Soc.*, **35** (1879), 406.

(3) C. Pehkschen, *J. Chem. Soc.*, **90** (1891), 88; *J. Pharm.*, (5), **22**, 265; *Pharm. Zeit. Russ.*, **29**, 339.

(4) Salzberger, *Arch. Pharm.*, **228** (1890), 462.

The so-called resinous matters in the roots of *Veratrum grandiflorum Loes. fil.* may, therefore, be considered as a mixture of salt-like substances, consisting of alkaloids, acids, and free phenolic substances. The chief constituents of the salt-like substances are probably molecular compounds of alkaloids and phenolic compounds, while the acids, soluble in water, are combined with the alkaloids as esters.

Experiments concerning the constitution of the phenolic compounds and the isolation of other alkaloids in crystalline state are in progress.

Experimental.

Treatment of the so-called resinous matters with dilute acetic acid. After the extraction[5] of the alkaloids from the powdered roots (12 kg.) with alcohol (95%) the solvent was distilled off under reduced pressure; a semi-solid residue was obtained. On treating the latter with water and light petroleum (b.p. 40–60°) a comparatively large amount of dark resinous matters, insoluble in water, separated and were collected. They were then digested successively with dilute acetic acid and with water to remove soluble basic substances and alcohol that had been absorbed. The brown powder thus obtained was next suspended in three parts of dilute acetic acid, and the mixture was stirred all day long and filtered. On basification of the filtrate with ammonia, free alkaloids were separated, which were collected, washed, and dried. The yield was 9.1 g. The amounts of the crude alkaloids obtained in each treatment were as follows:

Number of extraction	I	II	III	IV
Basic substances in g.	2.8	2.3	2.1	1.9

As may be seen from the table extraction proceeds very slowly, so that it was given up when the yield of the bases reached 0.5% of the material. At the later stage of the treatment the insoluble powder appeared to be partly decomposed by the dilute acetic acid. The yield of the insoluble powder was 302 g. or 2.5% of the roots.

The powder is sparingly soluble in water, light petroleum, and benzene; partly soluble in carbon tetrachloride, ether, acetic ester, and acetone; freely soluble in methyl and ethyl alcohol, and glacial acetic acid. When the powder is treated with dilute alcohol, in which it is sparingly soluble, it becomes viscous and resinous in appearance but can be restored by suspension in water, the absorbed alcohol being lost.

Alkaloids extracted with dilute acetic acid. This part of the alkaloids may be considered as a mixture of the bases described as portion A in Part I and those obtained from the insoluble part through hydrolysis.

Crude bases (34 g.) were dissolved in 0.5 N acetic acid (108 c.c.), diluted with water (108 c.c.) and divided into five parts by fractional precipitation with 0.5 N ammonium hydroxide. The first fraction was small in amount and brown in colour, but the amounts

(5) Compare Part I, this Bulletin, **9** (1934), 17.

of the second and third fractions were larger. The amounts of the fourth and fifth fractions were again small. To the mother liquor of the fifth fraction an excess of ammonia was added, when some more precipitates separated and were collected as the sixth fraction. The filtrate of the sixth fraction was saturated with ammonium sulphate and was extracted with chloroform. On working up the chloroform solution the seventh fraction was obtained. Each fraction thus obtained was then dissolved in alcohol and treated with hydrochloric acid in the same solvent. On being allowed to stand for a while, a crystalline hydrochloride, melting at 308° with decomposition, separated from the first, second, third, and fourth fractions. This was collected and dried; the yield was 5.6 g. or 16% of the crude bases. The salt (5.6 g.) was suspended in hot alcohol (90%, 62 c.c.) and was treated with sodium carbonate; on cooling the solution the freshly liberated base separated in colourless needles. It was collected and recrystallised from alcohol; it melted at 242–243°, and was proved to be jervine by mixed melting point with an authentic specimen. (Found: C, 75.70; H, 9.25. Calc. for $C_{26}H_{37}NO_3$: C, 75.86; H, 9.07%. $[\alpha]_D^{21°} = -150°$ in absolute alcohol.)

In the following table the amounts of each fraction as well as the yield of the salt are shown.

Number of fraction	I	II	III	IV	V	VI	VII
Precipitate in g.	0.3	14.8	5.3	0.1	0.1	0.4	1.5
Jervine hydrochloride in g.	0.1	4.2	1.3	trace	0	0	0

Treatment of the part insoluble in dilute acetic acid with ether. In order to remove fats and oils, free phenolic substances, and free alkaloids, the brown amorphous powder was treated first with dilute acetic acid and subsequently with ether for 26 days continuously. In the earlier stage of the process extraction proceeded fairly rapidly and a yellowish brown crystalline powder was obtained but its amount decreased gradually as the days passed. In the latter stage of the extraction brown viscous substances were obtained. After 10 days 0.5% of the material was extracted in 24 hours, while on the 24th day 0.1%. Total extract in 26 days was 55 g. or 18% of the material. On treatment of the extract with light petroleum (b.p. 40–60°) about 10 g. or 19% of fats and oils were removed, leaving a yellowish brown fine powder. The latter contained a trace of nitrogen, and was sparingly soluble in sodium bicarbonate, partly soluble in sodium carbonate, and almost perfectly soluble in caustic alkali. In water, light petroleum, chloroform, and benzene, it was difficultly soluble while freely soluble in methyl, ethyl alcohol, and acetic ester. It was crystallised from dilute alcohol in plates melting at 262° with decomposition. Its alcoholic solution gave a dark brown colouration with ferric chloride; it decolourised bromine water and potassium permanganate. On dissolving it in concentrated sulphuric acid it developed a colouration similar to the case of bromine water.

Decomposition of the part insoluble in dilute acetic acid with alkali. The amorphous brown powder (247 g.) purified as described above was treated with dilute alkali (1000 c.c.) when the solution rapidly turned dark brown in contact with the air owing to the absorption of oxygen, while the compact brown powder passed into lighter,

coarse, floating *bases*. After a while they were collected, washed, and dried in the air. The yield was 137 g. or 1.1% of the roots. The filtrate was saturated with carbon dioxide, when brown *phenolic substances* separated, which were collected, washed, and dried. On being treated with dilute sulphuric acid some more acidic substances were obtained. The yield of the phenolic and acidic substances altogether was 58 g. Lastly the filtrate was treated with ether continuously and *soluble acids* were extracted (ca. 26 g.). These phenolic and acidic substances rapidly turned dark brown in contact with the air through autoxidation either in an alkaline solution or in a solid state with a trace of alkali and moisture, but were comparatively stable if they were quite free from alkali as well as from moisture.

Phenolic substances. The brown phenolic substances contained no nitrogen and were comparatively difficultly soluble in ether; they gave off carbon dioxide on pyrogenetic treatment and appeared to be a phenolic acid.

Soluble acids. Among these acids angelic acid was detected. Another acid, melting at 102°, was very small in amount and was not further investigated.

Alkaloids. The bases obtained from the brown powder insoluble in dilute acetic acid had a characteristic odour and were partly soluble in benzene, ether, chloroform, acetic ester, and acetone, but sparingly soluble in light petroleum. In methyl and ethyl alcohol they were freely soluble.

Crude bases (88 g.) were dissolved in 0.5 N acetic acid (440 c.c.), the solution, after filtered from the insoluble matter, was diluted with water (440 c.c.), and the bases were fractionally precipitated. The results were similar to the other case of the fractional precipitation. Each fraction was treated with alcoholic hydrochloric acid, and jervine hydrochloride was isolated from the first to the fourth fraction; the yield was 32.8 g. or 37% of the crude bases, and 0.43% of the material. Taking into account the salt in Part I, the total yield of jervine hydrochloride amounted to 0.6% of the roots.

Number of fraction	I	II	III	IV	V	VI	VII
Precipitate in g.	4.0	25.9	40.0	1.4	0.6	0.7	1.3
Jervine hydrochloride in g.	1.5	12.5	18.8	trace	0	0	0

On treating the salt with sodium carbonate the free base was liberated and was crystallised from alcohol in colourless needles, melting at 242–243°, identified with jervine.

We are deeply indebted to Mr. K. Akagi, the Director of the Industrial Experiment Station at Kotoni near Sapporo, and Mr. K. Hayashi, the chief chemist of the institute, for affording us facilities for the investigation.

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ON THE ALKALOIDS OF WHITE HELLEBORE. III. EXPERIMENTS ON THE CONSTITUTION OF JERVINE.

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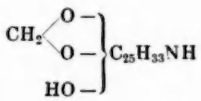
In Parts I[1] and II[2] it has been shown that the constituent alkaloids of *Veratrum grandiflorum Loes. fil.* can be extracted in a yield of 2.6% referring to the roots and from these alkaloids jervine hydrochloride may be isolated in a pure state in a yield of 23%, or 0.6% of the material. In the present communication some experimental results concerned with the constitution of jervine are given.

Jervine reacts as a secondary base giving a *N*-methyl derivative on methylation with diazomethane or better with methyl iodide and potassium hydroxide. Treatment of the latter with an excess of methyl iodide in a sealed tube gives a crystalline methiodide, while the same derivative can be obtained directly from jervine by boiling with methyl iodide and anhydrous potassium carbonate. Further evidence of this is afforded by the formation of a nitroso-compound on treatment of the alkaloid with sodium nitrite and acetic acid.

Jervine contains neither methoxyl nor carbonyl group and does not form an oxime or semicarbazone. Two oxygen atoms of the base appear to be present in the form of dioxymethylene, while the last one is in the form of an alcoholic hydroxyl group. The alkaloid dissolves in strong sulphuric acid, forming a yellow solution which becomes green on standing. It gives, however, reddish brown colouration with strong sulphuric acid together with phloroglucinol. On boiling with acetic anhydride the alkaloid yields a diacetyl derivative, melting at 176–177°, while it gives a monoacetyl compound, melting at 161–162°, with the same reagent but at room temperature. The former has been proved to be *O*, *N*-diacetyljervine and the latter to be *N*-acetyljervine. The *N*-methyl compound gives a monoacetyl derivative which melts at 186–187° at the boiling point of the reagent. On the other hand it furnishes no acetyl derivative at room temperature. At room temperature, therefore, the acetylation of jervine occurs at nitrogen but at the boiling point of acetic anhydride at both nitrogen and oxygen. The

(1) This Bulletin, **9** (1934), 15.
(2) *Ibid.*, **11** (1936), 168.

diacetyljervine is hydrolysed in steps as in the case of diacetyl-iso-yohimbine[3]. On hydrolysis with dilute and concentrated alcoholic caustic soda the acetyl compound furnishes the *N*-acetyl derivative and jervine respectively. Jervine has also been treated with acetic anhydride and anhydrous sodium acetate but the results are just the same as in the case of acetic anhydride only.



The functions of oxygen and nitrogen atoms of jervine have now been revealed as having two active hydrogen atoms, one in the hydroxyl and the other in the imino group. These were supported further by the results of determination of active hydrogen atoms after Zerewitinoff. Jervine may, therefore, be represented by the extended formula shown above.

Experiments concerned with the degradation of jervine are in progress.

Experimental.

Purification and properties of jervine. The alkaloid was stated by the earlier investigators to melt at various temperatures[4] and to give different colouration, showing that the purity of the base was doubtful. Jervine is present in nature with many other alkaloids which are hardly crystallisable. Consequently the specimen purified by the usual method may accompany more or less another veratrum alkaloid. In view of the minor alkaloids mixed with jervine the purification of the base was fundamentally tried. Taking advantage of the easiness with which the minor alkaloids could be decomposed, it was warmed with alcoholic potash when the impurities passed into solution in brown colour. The solution was concentrated and water was added: the base separated was collected, washed, and dried. This was crystallised from alcohol, forming colourless needles, melting at 243.5–244.5°[5]. The base in this purity may also be obtained through repeated recrystallisation from alcohol or acetic ester. Jervine thus purified showed $[\alpha]_D^{21°} = -150°$ in absolute alcohol (see Part I).

Pure jervine gives no colouration with concentrated hydrochloric acid but a specimen melting at 240–241° furnishes a yellow colour reaction. The colour reaction of jervine of inferior quality with strong sulphuric acid was described by Wright and Luff[6]. Pure jervine, melting at 243.5-244.5°, dissolves in cold strong sulphuric acid to a yellow fluid which in a very short time successively becomes orange, green, and then decolourises after several hours, whilst the impure specimen leaves a red solution instead of decolourisation. On dilution of the coloured solution it becomes colourless but may be reversed by adding strong concentrated sulphuric acid. When jervine was kept in the air it

(3) G. Hahn and W. Schuch, *Ber.*, **62**B (1929), 2953.

(4) Will: 200°, *Ann.*, **35** (1840), 117. Pehkschen, *J. Chem. Soc.*, **90** (1891), 88; *J. Pharm.*, (5), **22**, 265; *Pharm. Zeit. Russ.*, **29**, 339. Wright and Luff: 237–239°, *J. Chem. Soc.*, **35** (1879), 411. Salzberger: 238–242°, *Arch. Pharm.*, **228** (1890), 462. Bredemann: 241°, *Chem. Zentr.*, **1906**, I, 607; *Apoth. Ztg.*, **21**, 41.

(5) On melting it decomposes slightly and the m.p. depends more or less upon the rate of heating. It was determined by the bath preheated to 180°.

(6) Wright and Luff, *J. Chem. Soc.*, **35** (1879), 410.

became impure, colouring pale yellow with a depression of melting point. For instance, it melted unsharply at 239–240° after 7 days and at 220–229°, sintering at 160°, after 7 months. The specimen, however, in a closed vessel could be kept stable, and was found quite pure after 2 years.

Methylation of jervine with diazomethane. To a solution of jervine (0.5 g.) in methanol (50 c.c.) was added an ethereal solution of diazomethane prepared from nitrosomethylurethane (2 c.c.). On allowing to stand overnight, the solvents were removed, leaving a crystalline mass. This was treated with ether to remove the unchanged substance. On distilling off the solvent, *N*-methyljervine was left in colourless crystals (0.3 g.); it crystallised from dilute alcohol, m.p. 201–202°. It was shown to have 1 mol of water of crystallisation. (Found for air dry crystals on dehydration at 120° and 20 mm.: H_2O, 4.22, 4.02. Calc. for $C_{26}H_{36}O_3N$-CH_3·H_2O: H_2O, 4.07%. Found for dehydrated substance: C, 76.56; H, 9.17; -CH_3, 3.79. Calc. for $C_{26}H_{36}O_3N$-CH_3: C, 76.18; H, 9.24; -CH_3, 3.53%.)

The behaviours of methyljervine toward organic solvents are similar to those of jervine but the former is more soluble than the latter.

Methylation of jervine with methyl iodide and potassium hydroxide. Jervine (0.5 g.) in alcohol (12 c.c.) was heated with methyl iodide (1.4 g.) and potassium hydroxide (0.7 g.) for two hours on the water bath. After cooling, potassium iodide separated, which was filtered off, and the solvent was then removed. The residue was collected by means of water and dried. The yield was 0.5 g. This was crystallised from dilute alcohol in colourless crystals, m.p. 201–202°. There was no depression of melting point on admixture with *N*-methyljervine prepared by methylation with diazomethane. (Found: -CH_3, 3.87. Calc. for $C_{26}H_{36}O_3N$-CH_3: -CH_3, 3.53%.)

N-Methyljervine methiodide and methochloride. *N*-Methyljervine (0.5 g.) was heated in a sealed tube with methyl iodide (1 c.c.) at 100° for 6 hours. After cooling the excess of methyl iodide was distilled off when *N*-methyljervine methiodide separated in rosettes, melting at ca. 247°. It was dissolved in dilute alcohol and treated with moistened silver chloride. The silver iodide produced was filtered off and the filtrate evaporated, leaving a crystalline mass melting at 245° with decomposition. This is freely soluble in methanol and dilute alcohol, and sparingly soluble in ether and light petroleum. It recrystallised from absolute alcohol in needles melting at 252° with decomposition. The dried substance was analysed. (Found: Cl, 7.13. Calc. for $C_{26}H_{36}O_3N$-CH_3·CH_3Cl: Cl, 7.45%.)

The methiodide and methochloride are freely soluble in most organic solvents, especially in dilute alcohol, but they are insoluble in ether and light petroleum.

Treatment of jervine with methyl iodide and anhydrous potassium carbonate. A solution of jervine (0.5 g.) in methanol (10 c.c.) was heated with methyl iodide (1.4 g.) and anhydrous potassium carbonate (0.6 g.) on the water bath for 3 hours. It was cooled and the inorganic salt was filtered off. On removing the solvent a crystalline mass was separated; it was collected, washed, and dried. The yield was 0.6 g., m.p. 247° with decomposition. This was converted into the methochloride by treating with silver chloride as in the other case. The methochloride thus obtained, melting at 252° with decomposition, was proved to be identical with the chloride described above.

Nitrosojervine. Jervine (0.5 g.) in 2 N acetic acid (5 c.c.) was treated with sodium nitrite (0.1 g.) in water (1 c.c.) when crystalline powders separated. These were collected,

washed, and dried. The yield was 0.5 g. After repeated crystallisation from alcohol it melted at 251–252° with decomposition. (Found: N, 6.44. Calc. for $C_{26}H_{36}O_3N$-NO: N, 6.36%.)

Tetrahydrojervine. A solution of jervine (2 g) in pure glacial acetic acid (10 c.c.) was shaken in hydrogen with platinum oxide (0.42 g.). Absorption of hydrogen occurred at room temperature but it was rather slow; 198 c.c. or 1.98 mols were taken up in 24 hours. For the first one mol it took ca. 80 minutes but for the second ca. 22 hours. The solution was diluted with water, and the catalyst was removed. Tetrahydrojervine was separated by making the filtrate alkaline, collected, and washed. The yield was 2.1 g. Tetrahydrojervine was freely soluble in most organic solvents with the exception of light petroleum. It was hardly crystallisable from usual organic solvents. A solution of tetrahydrojervine in benzene was treated with light petroleum until the solution was set in turbidity. On allowing the solution to stand tetrahydrojervine crystallised out in colourless needles which, after drying, melted at 208–210°. The hydrochloride in needle crystals was made by treating an alcoholic solution with hydrochloric acid in the same solvent. It did not melt at 360°. (Found: C, 69.10; H, 9.34. Calc. for $C_{26}H_{41}O_3N$·HCl: C, 69.57; H, 9.37%.)

N-Acetyljervine. Jervine (5 g.) was dissolved in acetic anhydride (50 c.c.), and was allowed to stand overnight. The reaction mixture was treated with water, and a crystalline mass separated. This was collected and dried. The yield was 5.3 g. It was crystallised from dilute alcohol in stout crystals, melted at 161–162° with immediate foaming. (Found: C, 70.88, 70.63; H, 9.01, 9.15. Calc. for $C_{28}H_{43}O_4N·H_2O$: C, 71.29; H, 8.77%. The air-dried substance lost 4.02% at 115° and 16 mm. Calc. for $C_{28}H_{39}O_4N·H_2O$: 3.82%. Found for anhydrous substance: C, 74.23; H, 8.68%. Calc. for $C_{28}H_{39}O_4N$: C, 74.11; H, 8.67%.)

It is soluble in methyl alcohol, ethyl alcohol, acetone, chloroform, acetic ester, and benzene, but sparingly soluble in ether and light petroleum.

Diacetyljervine. A solution of jervine (5 g.) in acetic anhydride (50 c.c.) was boiled on the wire gauze 1.5 hours. The excess of the acetic anhydride was distilled off under reduced pressure and the trace of the latter was removed by treating with methyl alcohol; a syrupy substance was obtained. This was then treated with water when the acetylated compound separated in crystals. It was collected, washed, and dried. The yield was 5.95 g. It was recrystallised from dilute alcohol, rosettes, m.p. 176–177°. (Found: C, 73.14, 73.17; H, 7.75, 8.23. Calc. for $C_{30}H_{41}O_5N$: C, 72.68; H, 8.34%.)

It is soluble in methyl alcohol, ethyl alcohol, acetone, acetic ester, chloroform, and benzene, but sparingly soluble in ether and light petroleum.

Hydrolysis of diacetyljervine. A solution of diacetyljervine (0.23 g.) in alcohol (14 c.c.) was treated with 0.1 N alcoholic caustic soda and was warmed for 4 hours on the water bath. On evaporation a crystalline mass (0.15 g.) was obtained; it was collected by means of water and dried. It was recrystallised from dilute alcohol, six-sided plates, m.p. 158–159° with decomposition. The hydrolysed substance was proved in every point to be *N*-acetyljervine described above. This was treated once more with the same but more concentrated reagent The mixture was heated for 6 hours. On working up the reaction mixture jervine was obtained. Moreover diacetyljervine was also treated with concentrated alcoholic caustic alkali as above, jervine being obtained in one step.

Acetylation of N-methyljervine. *N*-Methyljervine prepared by the method described above was treated with acetic anhydride in the cold as in the case of jervine. On working up, the starting substance was recovered unchanged.

O-Acetyl-N-methyljervine. *N*-Methyljervine (0.3 g.) was dissolved in acetic anhydride (10 c.c.) and was kept boiling for an hour. The excess of acetic anhydride was removed under diminished pressure and the reaction product, on treating with water, was collected, washed, and dried. After crystallisation from dilute alcohol, needle crystals in rosettes melted at 186–187°. The yield was 0.07 g. (Found : C, 74.50 ; H, 8.96. Calc. for $C_{29}H_{41}O_4N$: C, 74.47 ; H, 8.84%.)

It is soluble in most organic solvents with the exception of light petroleum.

Determination of active hydrogen. Active hydrogen in jervine was determined by the method of Zerewitinoff using pyridine[7] as the solvent (Found : active hydrogen, 0.54% or 2.17 atoms. Calc. for 2H in $C_{26}H_{37}O_3N$: 0.49%).

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A NEW BACTERIOXANTHOPHYLL, THE YELLOW PIGMENT OF SARCINA LUTEA.[1]

(Preliminary Report.)

By **Teruko NAKAMURA.**

Received October 29th, 1935. Published March 28th, 1936.

In recent years, inquiries into the chemical nature and biological significance of organic colouring matters have been made to a great extent, but very few pigments of microorganisms have been studied chemically. The chemical nature of most of the pigments in highly coloured bacteria is not well known, although its study would be of interest not only for the understanding of the biological rôle of the bacterial pigments themselves, but also for comparison in cases of pigments which are also found in higher plants.

The writer has studied the yellow pigment of *Sarcina lutea*[1] which is prevalent in air. Although the occurrence of carotenes in bacterial pigments

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(7) Th. Zerewitinoff, *Ber.*, **47** (1914), 2417.

(1) After the completion of this manuscript, the author has found a note on the pigment of *Sarcina lutea* : E. Chargaff and J. Dieryck, *Naturwiss.*, **20** (1932), 872.

is generally accepted and moreover demonstrated by absorption spectra[2] and by feeding experiments[3] for the vitamin A activity, reports on the examination of carotenoids isolated as such from any bacterial growth are still meager.

The pale yellow pigmentation of *Sarcina lutea* with green fluorescence which is distinct from well known red or orange coloured carotenoids, e.g. lycopene or carotenes, seemed to furnish a new interesting material for study. The pigment was found to be carotenoidal, containing chiefly a xanthophyllic substance which gave ordinary lipochrome reactions and which revealed absorption maxima at 490, 460, and 433mμ in carbon bisulphide. The study of such hitherto undefined yellow pigment of microorganism is of interest in connection with the investigation of xanthophyllic matter in higher plants as they are conjectured to be the precurser of carotenes. The present paper is a preliminary report.

Experimental.

Isolation of the Pigment. The organism was grown on broth agar at 22°.[4] The medium was slightly alkaline (*p*H 7.2). A solid culture was preferred to a liquid medium because on agar it was found to grow more rapidly and also to produce more pigment. The organism reached maximum pigmentation in approximately 10 days, when the growth was scraped off the surface.

The pigment was collected as follows: The cultures were extracted with cold 98% methyl alcohol in the dark at room temperature, until the cellular material became almost colourless; the pigment was taken up as a clear yellow methyl alcoholic solution with green fluorescence. The alcoholic solution was then distilled to dryness in a stream of CO_2 gas at 5-° under a diminished pressure. The residue consisted of a greenish yellow matter. It was washed with a small quantity of methyl alcohol which dissolved the pigment leaving a great portion of a white residual matter undissolved. The latter was readily soluble in water and sparingly soluble in organic solvents.

The methyl alcoholic solution of the pigment was concentrated by distillation and was diluted with water until it contained 30% methyl alcohol, and the solution was extracted with ether. From the ether extract, the solvent was removed, leaving the crude pigment of greenish yellow colour, which was tested chemically and spectroscopically.

Solubility. Insoluble in H_2O, in aqueous acid (HCl), and alkaline solutions (NaOH), soluble in methyl alcohol, ethyl alcohol, ether, chloroform, carbon bisulphide, acetone, benzine, benzene, petroleum ether, and xylene. Among the above solvents it is most soluble in methyl alcohol and only slightly soluble in petroleum ether and benzine.

Colour Reactions. Blue colourations with conc. H_2SO_4, with $SbCl_3$, and with chloroacetic acid in chloroform. No colouration with 25% HCl, conc. HCl, HNO_3, acetic acid,

(2) V. Reader, *Biochem. J.*, **19** (1925), II, 1041.
(3) Carl A. Baumann, H. Steenbock, Mary A. Ingraham, and E. B. Fred, *J. Biol. Chem.*, **103** (1933), 339.
(4) On the improved method of cultivation, a report will be made by Mr. R. Ohtake.

and phosphoric acid. On addition of HCl or NaOH to the alcoholic solution no appreciable change was obs rved in the colour.

Oxidation and Reduction. The alcoholic solution was decolourized by Mg and HCl, and by H_2O_2 on standing.

Adsorption Tests. From the ether or benzine solution, the pigment could be adsorbed on several substances, e.g. Al_2O_3, kaolin, silica, fuller's earth, and "Faserton-erde" (Fränkel), but not on $CaCO_3$.

The elution of the adsorbed pigment, however, was difficult. Only in the cases of Al_2O_3 and "Faserton erde" the pigment could be separated in 1–5% solution of methyl alcohol in petroleum ether or benzine. This behavior is comparable with that of cryptoxanthine.(5)

Spectroscopic Measurements. With a hand spectroscope the following absorption maxima were read:

Solvent	Absorption maxima (mμ)		
Carbon bisulphide	490	460	(433)
Chloroform	475	445	(423)
Alcohol	467	436	(410)
Methyl alcohol	468	435	(408)
Ether	468	437	(413)
Benzine	470	440	

The third maximum placed in brackets was not distinct.

The spectrographic readings are lower than in any of the already identified carotenoids. Among similar compounds, the nearest values found in the literature are those of a short wave xanthophyll (468–469, 438–439 in alcohol),(6) β-xanthophyll of Tswett which is noted by Kuhn, and of canary xanthophyll(7) (472, 443, 418 in benzine). But as already mentioned the pigment of *Sarcina lutea* is not adsorbed on $CaCO_3$, while β-xanthophyll is.

Saponification. A solution of the pigment in methyl alcohol was saponified with alcoholic potash, the concentration of the alkali being 2.5%. It was kept at 50° for 2 hours in a stream of hydrogen. On expelling a portion of the alcoholic solvent by distillation, the pigment became soluble in water. From the aqueous solution it could not be extracted with ether. On acidifying, however, the pigment was taken up in ether. It was also possible to extract the pigment with ether after saturating the alkaline solution of saponification with a stream of CO_2.

Notes. Minute quantity of a yellow crystalline substance was obtained from benzine and acetone solutions of the pigment. Further work is in progress to obtain the pigment

(5) R. Kuhn and C. Grundmann, *Ber.*, **66** (1933), 1746.
(6) R. Kuhn and H. Brockmann, *Z. physiol. Chem.*, **206** (1932), 60.
(7) H. Brockmann and O. Völker, *Z. physiol. Chem.*, **224** (1934), 209.

in pure crystalline state by the method of chromatograph ;[8] thereby the pigment may be divided into components.

Summary.

The yellow pigment of *Sarcina lutea* was examined. It is a lipochromic substance with absorption maxima at 490, 460, and 433 mμ in carbon bisulphide apparently distinct from well known xanthophylls, the constitution of which had not been identified. Saponification showed the substance to be chiefly a xanthophyll-like ester. The work is being continued.

The author wishes to express her sincere thanks to Prof. R. Majima and to Dr. C. Kuroda for their advice and encouragement throughout this work. She is grateful to Prof. U. Suzuki for his kind interest. She is also indebted to Dr. T. Kodama of the Kitasato Institute for Infectious Diseases for furnishing her with the pure strain of *Sarcina lutea* and to Mr. R. Ohtake for the most valuable assistance rendered to her in the cultivation of the organism.

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Chemical Research.

SYNTHESIS OF 4-HYDROXY-3-ETHOXY-1-ALLYL-BENZENE FROM 4-HYDROXY-3-METHOXY-1-ALLYL-BENZENE (EUGENOL).

By Nenokichi HIRAO.

Received October 31st, 1935. Published March 28th 1936.

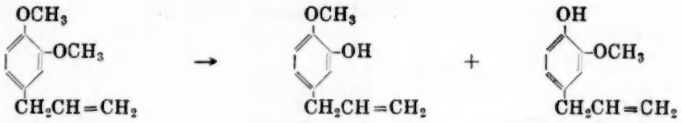
On the basis of Grignard's reaction the author prepared eugenol and chavibetol from eugenol methyl ether[1], isoeugenol and isochavibetol from isoeugenol methyl ether[1], safroeugenol from eugenol ethyl ether[1], isosafroeugenol from isoeugenol ethyl ether[1], and 4-hydroxy-3-ethoxy-1-propenyl-benzene[2] from isochavibetol ethyl ether[3].

(8) R. Kuhn and H. Brockmann, *Z. physiol. Chem.*, **206** (1932), 41. A. Winterstein and G. Stein, *Z. physiol. Chem.*, **220** (1933), 247.

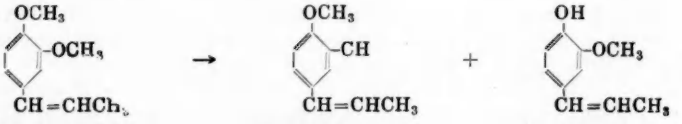
(1) *J. Chem. Soc. Japan*, **52** (1931), 519.

(2) The author proposes to designate Isohomogenol.

(3) *J. Chem. Soc. Japan*, **52** (1931), 263.



Eugenol methyl ether — Chavibetol — Eugenol



Isoeugenol methyl ether — Isochavibetol — Isoeugenol

Eugenol ethyl ether — Safroeugenol

Isoeugenol ethyl ether — Isosafroeugenol

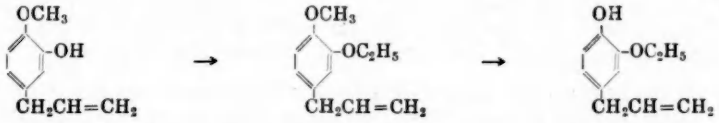
Isochavibetol ethyl ether — Isohomogenol

It has been considered difficult to prepare chavibetol, but the author synthesised it with ease by the above method. The mixture of chavibetol and eugenol was readily separated in their benzoates by fractional recrystallisation from petroleum ether and alcohol in turn.

Chavibetol ethyl ether, a new compound, was prepared by the ethylation of chavibetol with a good yield. It had the following constants: b.p. 114°/6.5 mm., d_4^{25} 1.0073, n_D^{25} 1.5231. On oxidation with potassium permanganate 4-methoxy-3-ethoxy-benzoic acid, m.p. 162–163°, was formed.

4-Hydroxy-3-ethoxy-1-allyl-benzene, a new compound, was prepared in a good yield by the action of Grignard's reagent on chavibetol ethyl ether. The author proposes to designate this new compound "homogenol." It is a

clear liquid with an odour resembling eugenol. In alcoholic solution a green colouration was observed upon the addition of ferric chloride.



Chavibetol — Chavibetol ethyl ether — Homogenol

Homogenol had the following physical constants: b.p. 114.5°/8.5 mm.; d_4^{25} 1.0344, n_D^{25} 1.5292; benzoate, m.p. 45.5°; phenylurethane, m.p. 93.5–94.5°. (Further experiment on the same line is now in progress.)

Experimental.

(1) **Action of Grignard's reagent on eugenol methyl ether.** (a) A solution of 9 g. of eugenol methyl ether in 10 g. of xylene was poured into Grignard's reagent prepared from 1.3 g. of magnesium 8 g. methyl iodide, and 10 g. of dry ethyl ether. The mixture was heated on the oil bath at 160–180° for 2 hours under a reflux condenser. After cooling to room temperature some pieces of ice and dilute acetic acid were added, and the reaction product was distilled in steam. The distillate was extracted with ether and washed with a dilute solution of sodium bicarbonate. Seven grams of a phenolic substance and 0.2 g. of a neutral oil were obtained by shaking with dilute caustic soda in usual manner. The phenolic product had a sweet taste, and the presence of chavibetol was suspected.

(b) *Isomerisation.* One part of the phenolic product and 2 parts of potassium hydroxide were mixed in a test tube, and heated on the oil bath at about 220° for one hour. The mass was dissolved in water and acidified. The crude product was obtained is a yield more than 90 per cent of theory. One part was dissolved in 3 or 4 parts of hot 50% alcohol, and then cooled to room temperature. Isochavibetol crystallised out in glistening thin plates, m.p. 95–96°, and was confirmed by mixed melting point with an authentic specimen.

(c) *Separation of eugenol and chavibetol in their benzoates.* The phenolic product (b.p. 128–129°/6 mm.) (42 g.) was added to a solution of 19 g. of potassium hydroxide and (110 g.) of alcohol, and the solution was cooled with ice. Benzoyl chloride (43 g.) was added in a thin stream with constant stirring. When the reaction was completed, about 500 c.c. of water was added and the separated benzoates collected and washed with water. The benzoates were added to 80 c.c. of hot alcohol, and on cooling 87 g. of crystals were obtained. The crystals were dissolved in 200 c.c. hot petroleum ether (b.p. 30–60°), and, on standing, 10.3 g. of magnificent crystals appeared. The melting point of these crystals was 69°, and they were identified as eugenol benzoate by mixed melting point with an authentic specimen.

About a quarter of the solvent in the mother liquor was distilled off, and then it was allowed to crystallise, when 6.5 g. of crystals, m.p. 49°, separated, which differed

from the former. They were chavibetol benzoate. The mother liquor was evaporated to half its volume, when 23 g. of crude product, m.p. 42–62°, crystallised. This is a mixture of the two benzoates. When 1 part of this mixture was treated with 2.5 parts of hot petroleum ether a small quantity of eugenol benzoate remained in crystalline state, and relatively pure chavibetol benzoate crystallised out from the solution. On repetition, it proved possible to separate the two benzoates from the mixture.

(2) **Action of Grignard's reagent on isoeugenol methyl ether.** (a) *Isoeugenol methyl ether.* To the reaction mixture of 32.8 g. of isochavibetol, m.p. 95°, 15 g. of potassium hydroxide and 30 c.c. of water, some pieces of ice and 25.2 g. of dimethyl sulphate were added, and then the mixture was shaken mechanically. The methylated product was treated in the usual manner. Yield 25.5 g.; b.p. 135°/14 mm.; d_4^{25} 1.0504; n_D^{25} 1.5655; M.R. 55.24; $C_{11}H_{14}O_2$ 52.22.

(b) A solution of 9 g. of isoeugenol methyl ether and 10 c.c. of xylene was added to Grignard's reagent prepared from 1.44 g. of magnesium, 8.5 g. of methyl iodide, and 10 c.c. of ether. After the usual procedure 6 g. of a phenolic product was separated. On recrystallisation from 50% alcohol 1.3 g. of isochavibetol, m.p. 94°, was yielded. Most of the residue of the mother liquor consisted of isoeugenol, which was confirmed by the formation of its benzoate melting at 103.5°.

(3) **Action of Grignard's reagent on eugenol ethyl ether. Synthesis of safroeugenol.** (a) *Eugenol ethyl ether.* Ethyl iodide (20.8 g.) and methanol (10 g.) were added to the reaction mixture containing 21.6 g. of eugenol, 10 g. of potassium hydroxide, and 7 c.c. of water. The mixture was boiled under a reflux condenser for an hour. Yield 22 g.; b.p. 122–125°/12 mm.; d_4^{25} 1.0099; n_D^{25} 1.5254.

(b) *Safroeugenol.* Eugenol ethyl ether and xylene (10 g.) were added to Grignard's reagent prepared from 1.3 g. of magnesium, 8 g. of methyl iodide, and 10 g. of ether. The usual treatment yielded 3.2 g. of a phenolic product. B.p. 129.5°/20 mm.; m.p. 34.5°; d_4^{25} 1.0335; n_D^{25} 1.5304 (in supercooled state); M.R. 53.23; $C_{11}H_{14}O_2$ 52.10. (Found: C, 73.88; H, 8.19. Calc. for $C_{11}H_{14}O_2$: C, 74.16; H, 7.87%.) Phenylurethane, m.p. ca. 58°.

Isomerisation. The phenolic product (0.5 g.) and potassium hydroxide (1 g.) were heated in a small test tube in the oil bath at 200° for one and a half hours. The reaction product was dissolved in water and acidified with acetic acid. Lustrous thin plates crystallised out, and after recrystallisation from 50% alcohol, they melted at 85°. They were isosafroeugenol, and identification was established by mixed melting point with an authentic specimen.

The above data show that the phenolic product is safroeugenol.

(4) **Action of Grignard's reagent on isoeugenol ethyl ether. Synthesis of isosafroeugenol.** (a) *Isomerisation of eugenol ethyl ether.* In a test tube 5 g. of eugenol ethyl ether and 5 g. of potassium hydroxide were heated in the oil bath at 200° for 2 hours. The reaction mixture was dissolved in water and the separated crystals were collected and washed with water. The yield of the crystals was 4.8 g. These white crystals melted at about 61°, and after recrystallisation from 90% alcohol the melting point was raised to 63°, identical with that of isoeugenol ethyl ether.

(b) *Isosafroeugenol.* Isoeugenol ethyl ether (4.7 g.) and xylene (15 g.) were added to Grignard's reagent prepared from 0.65 g. of magnesium, 3.8 g. of methyl iodide and 10 c.c. of ether. The mixture was treated as above, and 4.1 g. of a phenolic product was

produced in white crystals (theoretical yield 4.37 g.). Its melting point was 83°, but, after one recrystallisation from 50% alcohol, rose to 85°, identical with that of iso-safroeugenol.

(5) **Action of Grignard's reagent on isochavibetol ethyl ether. Synthesis of iso-homogenol.** (a) *Isochavibetol ethyl ether.* To the reaction mixture of 32 g. of isochavibetol, 12 g. of potassium hydroxide, and 20 c.c. of water, 37 g. of potassium ethyl sulphate was added, and the mixture was heated in the oil bath at 150–160° for 2 hours, and after cooling, a dilute solution of sodium hydroxide was added. Twenty three grams of white crystals were separated and readily purified by recrystallisation from 90% alcohol, m.p. 49.5° (Found: C, 74.84; H, 8.39. Calc. for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33%). On oxidation with 3% potassium permanganate solution 4-methoxy-3-ethoxy-benzoic acid, m.p. 162–163°, was formed, which was identified by mixed melting point with an authentic specimen. These data show that the white crystalline substance is isochavibetol ethyl ether.

(b) *Isohomogenol.* A solution of 6.4 g. of isochavibetol ethyl ether in 30 g. of xylene was added to Grignard's reagent prepared from 0.9 g. of magnesium, 5.5 g. of methyl iodide, and 10 c.c. of dry ether, and the mixture boiled for 2 hours under a reflux condenser. Two grams of a crystalline phenolic substance was produced, and recrystallised from 50% alcohol. It melted at 53–54°. (Found: C, 74.06; H, 7.97. Calc. for $C_{11}H_{14}O_2$: C, 74.16; H, 7.89%.) The melting point of its benzoate was 87°, identical with that of isohomogenol benzoate.

(6) **Action of Grignard's reagent on chavibetol ethyl ether. Synthesis of homogenol.** (a) *Chavibetol.* In alcoholic solution, 49 g. of the pure chavibetol benzoate, m.p. 49°, described above, was saponified with 18 g. of potassium hydroxide. Yield 23 g.; b.p. 113°/8 mm. (oil bath 130°); $d_{.5}^{25}$ 1.0646, d_4^{25} 1.0613; n_D^{25} 1.5379; M.R. 48.33; $C_{10}H_{12}O_2F_4$ 47.48.

(b) *Chavibetol ethyl ether.* In a pressure bottle, a solution of 23 g. of chavibetol, 9.3 g. of potassium hydroxide, 100 c.c. of alcohol, and 17 g. of ethyl bromide was heated at 80–90° on the water bath for 3 hours. Chavibetol (1.5 g.) was recovered. Yield 23.8 g.; b.p. 114°/6.5 mm. (oil bath 140°); d_{25}^{25} 1.0104, d_4^{25} 1.0073; n_D^{25} 1.5231; M.R. 58.23; $C_{12}H_{16}O_2F_4$ 56.83. (Found: C, 74.82· H, 8.45. Calc. for $C_{12}H_{16}O_2$: C, 75.00; H, 8.33%.) It had a faint odour. This ethyl ether (1.7 g.) was oxidised with 2.5% potassium hydroxide solution (200 c c.), the reaction mixture was filtered, and the filtrate acidified with acetic acid. 4-Methoxy-3-ethoxy-benzoic acid (m.p. 161–162°, 0.5 g.) was obtained as white crystals. It was identified by mixed melting point with an authentic specimen.

(c) *Homogenol.* The solution of the foregoing ethyl ether (23.8 g.) in xylene (30 c.c.) was added to Grignard's reagent prepared from magnesium (3 g.), methyl iodide (18 g.) and ether (50 g.), and the product treated in the usual manner. A phenolic product (homogenol 18.5 g.) was obtained. B.p. 112°/6.5 mm.; d_{25}^{25} 1.0375, d_4^{25} 1.0344; n_D^{25} 1.5292; M.R. 52.81; $C_{11}H_{14}O_2F_4$ 52.10. (Found: C, 73.89; H, 8.07. Calc. for $C_{11}H_{14}O_2$: C, 74.16; H, 7.89%.) It is a colourless oil with eugenol-like odour. In alcoholic solution a greenish tinge was given with ferric chloride.

Phenylurethane. After standing for 2 months, the mixture of homogenol (1 g.) and carbanil (0.9 g.) crystallised completely, and the product was recrystallised from 80% methanol, m.p. 93.5–94.5° (sharp). (Found: C, 72.55; H, 6.50. Calc. for $C_{18}H_{19}O_3N$: C, 72.73; H, 6.40%.)

Benzoate. In ice cooling, benzoyl chloride (1.4 g.) was added to a solution of homogenol (1.65 g.) and potassium hydroxide (0.7 g.) in alcohol (10 g.). Yield of crude benzoate, 3 g. On standing, the solution of the benzoate in petroleum ether gave beautiful plates, m.p. 45.5° (sharp). (Found: C, 76.25; H, 6.52. Calc. for $C_{18}H_{18}O_3$: C, 76.60; H, 6.38%).

Isomerisation. In a small test tube, homogenol (1.3 g.) and potassium hydroxide (1.5 g.) were heated on the oil bath at 180–200° for 2 hours. The reaction mixture was dissolved in water and the solution acidified with acetic acid, when white crystals separated out. Yield 1.1 g. Benzoate was prepared and recrystallised from alcohol, m.p. 85.5–86.2°. It is identical with the isohomogenol benzoate.

In conclusion, the author wishes to express his gratitude to Dr. Kashichi Ono for his kind guidance during this investigation.

Research Laboratory of
Saisei Shōnō Kabushiki Kaisha, Kobe.

STUDIES ON THE DERIVATIVES OF BENZOYLBENZOIC ACIDS.

By Mosuke HAYASHI, Sinzô TURUOKA, Ikuo MORIKAWA, and Hirochika NAMIKAWA.

Received October 31st, 1935. Published March 28th, 1936.

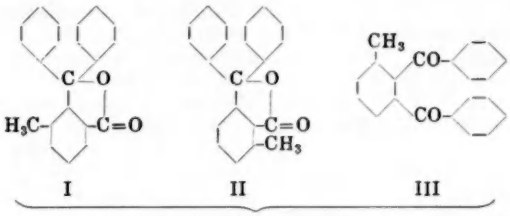
One of the authors has reported an isomeric change of halogenohydroxybenzoyltoluic acids under the influence of concentrated sulphuric acid[1]. They now wish to report further studies on the other derivatives of benzoylbenzoic acid.

I. **Condensation of 3-Methylphthalic Anhydride with Benzene.** When 3-methylphthalic anhydride was condensed with benzene, one substance, m.p. 116–117° (A), from the part insoluble in ammonia and two benzoyltoluic acids, m.p. 171–172° (B) and m.p. 126.5–127.5° (C), from the part soluble in ammonia were isolated. The analytical data of the first substance (A) corresponded to the empirical formula $C_{21}H_{16}O_2$, and it may be 1-methyl-2,3-dibenzoylbenzene (III) or diphenylmethylphthalide (I or II).

Benzoyltoluic acids (B and C) remained unaltered on being treated with concentrated sulphuric acid at room temperature. But when isomeride B was treated with concentrated sulphuric acid at 100–105°, an isomeric change

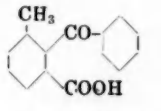
(1) *J. Chem. Soc.*, **1927**, 2516; **1930**, 1513, 1520,1524.

occurred, and isomeride C was obtained from the part soluble in ammonia. From the reason that stereoisomerides can not exist owing to their constitutions in this case, we must consider that benzoyltoluic acid B or C may have the formula IV or V and the action of concentrated sulphuric acid on isomeride B gives rise to position isomeric change. From this evidence, the isomeric phenomenon of the other benzoylbenzoic acid derivatives, which have already been reported in the previous papers,[1] should be a position isomeric change.



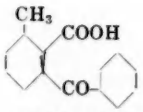
I II III

m.p. 116–117° (A)



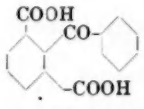
m.p. 171–172° (B)

IV



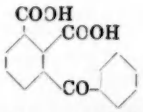
m.p. 126.5–127.5° (C)

V



m.p. 255–256° (D)

VI



Air dried, m.p. 121–125–146° (E)
Anhydrous, m.p. 140–141° (foam.)

VII

The diphenylketone dicarbonic acids, which were obtained by oxidizing benzoyltoluic acids B and C with potassium permanganate, melted at 255–256° (D) and at 121–125–146° (air dried) (E) respectively. Since diphenylketone-2,6-dicarbonic acid melts at 260°[2] and diphenylketone-2,3-dicarbonic acid at 100–130–140–183°[3], substances D and E would be diphenylketone-2,6-dicarbonic acid (VI) and diphenylketone-2,3-dicarbonic acid (VII); and accordingly benzoyltoluic acids B and C would be 2-benzoyl-3-methylbenzoic acid (IV) and 2-benzoyl-6-methylbenzoic acid (V), respectively.

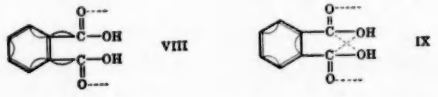
On assuming that the equilibrium of 3- and 6-isomeride in concentrated sulphuric acid solution would be much the same as in the cases of 2-benzoyl-3-methylbenzoic acid and the halogenohydroxytoluic acids, the halogenohydroxybenzoyltoluic acids which have been reported in the previous papers would have formulæ as shown in Table 1.

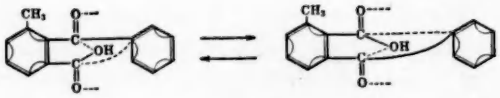
(2) Graebe and Leonhardt, *Ann.*, **290** (1896), 232.
(3) Graebe and Leonhardt, *ibid.*, 230.

Table 1.

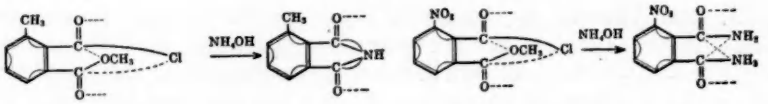
Original	Corrected
2-(5′-Chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid, m.p. 238–239°[4]	2-(5′-Chloro-2′-hydroxybenzoyl)-3-methylbenzoic acid
2-(5′-Chloro-2′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid, m.p. 171–171.5°[5]	2-(5′-Chloro-2′-hydroxybenzoyl)-6-methylbenzoic acid
2-(5′-Bromo-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid, m.p. 246–246.5°[6]	2-(5′-Bromo-2′-hydroxybenzoyl)-3-methylbenzoic acid
2-(5′-Bromo-2′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid, m.p. 163.5–164°[7]	2-(5′-Bromo-2′-hydroxybenzoyl)-6-methylbenzoic acid
2-(3′-Chloro-4′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid, m.p. 198–199°[8]	2-(3′-Chloro-4′-hydroxybenzoyl)-3-methylbenzoic acid
2-(3′-Chloro-4′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid, m.p. 188.5–189°[9]	2-(3′-Chloro-4′-hydroxybenzoyl)-6-methylbenzoic acid
2-(4′-Chloro-2′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid, m.p. 219.5–220.5°[10]	2-(4′-Chloro-2′-hydroxybenzoyl)-3-methylbenzoic acid
2-(4′-Chloro-2′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid, m.p. 177.5–178°[11]	2-(4′-Chloro-2′-hydroxybenzoyl)-6-methylbenzoic acid
2-(2′-Chloro-4′-hydroxybenzoyl)-3(or 6)-methylbenzoic acid, m.p. 218–218.5°[12]	2-(2′-Chloro-4′-hydroxybenzoyl)-3-methylbenzoic acid
2-(2′-Chloro-4′-hydroxybenzoyl)-6(or 3)-methylbenzoic acid, m.p. 201–202°[13]	2-(2′-Chloro-4′-hydroxybenzoyl)-6-methylbenzoic acid

Now that we consider that the formula of phthalic acid is IX instead of VIII, the above-mentioned phenomena and also the reaction of ammonia on acid chloride of alkyl 3- or 4-methylphthalate[14] and on acid chloride of methyl 3- or 4-nitrophthalate[15] may be conveniently illustrated as shown below.





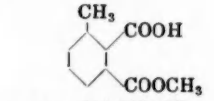
(4) (5) (6) (7) *J. Chem. Soc.*, **1927**, 2516; *ibid.*, **1930**, 1514.
(8) (9) *J. Chem. Soc.*, **1930**, 1521.
(10) (11) (12) (13) *J. Chem. Soc.*, **1930**, 1526.
(14) See pp. 187, 193.
(15) See pp. 191, 200; *J. Soc. Chem. Ind., Japan*, **36** (1933), 203B.



II. Condensation of Acid Chlorides of Methyl 3- and 4-Methylphthalates with Benzene. The methyl ester of benzene-1,2,3-tricarbonic acid, which was obtained by oxidizing methyl 3-methylphthalate (F), m.p. 114.5–115°, with potassium permanganate, melted with decomposition at 193–194°[16]. When acid chloride of methyl 3-methylphthalate (F) was condensed with benzene, 2-benzoyl-3-methylbenzoic acid (IV) and substance A (I, II or III) were obtained, but 2-benzoyl-6-methylbenzoic acid (V) could not be isolated. From these facts, it is highly probable that methyl 3-methylphthalate (F), m.p. 114.5–115°, may be 1-methyl 3-methylphthalate (X). Therefore, ethyl 3-methylphthalate (G), m.p. 86–87°, would be also 1-ethyl 3-methylphthalate (XI).

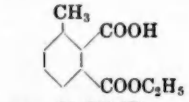
Benzoyltoluic acid, which was obtained by condensing acid chloride of methyl 4-methylphthalate (H), m.p. 89–90°, with benzene, melted at 136–138° and was proved to be identical with 2-benzoyl-5-methylbenzoic acid (XXII)[17]. Therefore, methyl 4-methylphthalate (H), m.p. 89–90°, may be 2-methyl 4-methylphthalate (XII).

On treating acid chloride of 1-methyl or 1-ethyl 3-methylphthalate and of 2-methyl 4-methylphthalate with conc. aqueous ammonia, 3-methylphthalimide (XIV), m.p. 188.5-189°[18] and 4-methylphthalimide (XV), m.p. 194.5–195°[19], were obtained, respectively[20].



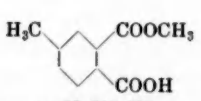
m.p. 114–115° (F)

X



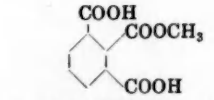
m.p. 86–87° (G)

XI



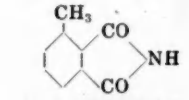
m.p. 89–90° (H)

XII



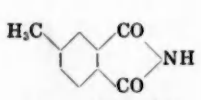
m.p. 203–205°(decomp.)

XIII



m.p. 188.5–189°

XIV



m.p. 194.5–195°

XV

(16) *Ann.*, **290** (1896), 226: 2-methyl ester of benzene-1,2,3-tricarbonic acid (XIII), m.p. 203–205° (decomp.).

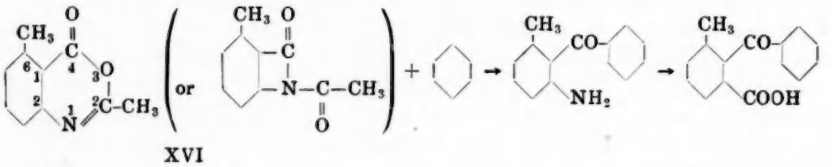
(17) *J. Chem. Soc.*, **1930**, 1518: 2-benzoyl-4 (or 5)-methylbenzoic acid (E), m.p. 145–145.5°, and also see p. 189 and 197.

(18) *Ber.*, **25** (1892), 2107; **40** (1907), 4413: m.p. 183–184°, 187°.

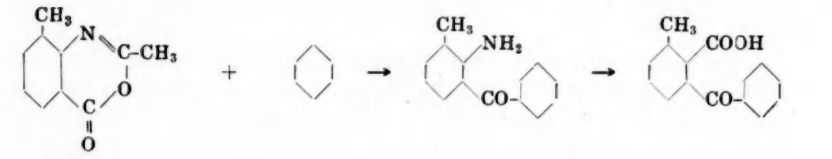
(19) *Monatsh.*, **12** (1891), 627: m.p. 196°.

(20) Compare p. 193.

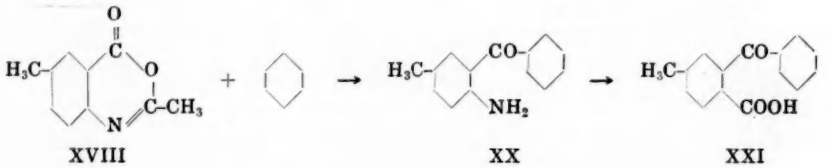
III. An Attempt to determine the Constitutions of Benzoyltoluic Acids. As far as the authors are aware, a condensation of methyl-2-oxo-4-(toluoxazine-3,1)-derivatives with aromatic hydrocarbons or with their derivatives in the presence of aluminium chloride has not been reported. This synthesis was attempted to determine the constitutions of benzoyltoluic acids by schemes shown below. The results were not very satisfactory, yields of amino-diphenylketones being very poor.



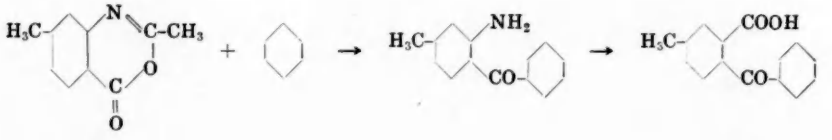
XVI



XVII



XVIII XX XXI

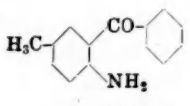


XIX XXII

2-Amino-5-methyldiphenylketone (XX) had been already prepared by Chattaway and Lewis[21], Esselen and Clarke[22], and Hanschke[23]. 2-Benzoyl-4-methylbenzoic acid (XXI), which was derived from 2-amino-5-methyldiphenylketone, melted at 149–150° and was proved to be identical with 2-

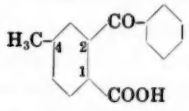
(21) *J. Chem. Soc.*, **85** (1904), 594.
(22) *J. Am. Chem. Soc.*, **1914**, 321.
(23) *Ber.*, **32** (1899), 2021.

benzoyl-(5 or 4)-methylbenzoic acid (D), m.p. 150-150.5°.[24] Therefore 2-benzoyl-(4 or 5)-methylbenzoic acid[17] (E), m.p. 145–145.5°, should be 2-benzoyl-5-methylbenzoic acid (XXII).



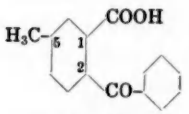
m.p. 64–64.5°

XX



m.p. 149–150° (150–150.5°)
[2-Benzoyl-5(or 4)-methylbenzoic Acid (D)]
2-Benzoyl-4-methylbenzoic Acid

XXI



m.p. 145–145.5°
[2-Benzoyl-4(or 5)-methylbenzoic Acid (E)]
2-Benzoyl-5-methylbenzoic Acid

XXII

By analogy the authors propose the corrections of the interpretations given in the paper, "A New Isomerism of Halogenohydroxybenzoyltoluic Acids" as shown in Table 2.

Table 2.

Original	Corrected
2-(5′-Chloro-2′-hydroxybenzoyl)-5(or 4)-methylbenzoic acid (A), m.p. 239.5–240.5°[25]	2-(5′-Chloro-2′-hydroxybenzoyl)-4-methylbenzoic acid (A)
2-(5′-Chloro-2′-hydroxybenzoyl)-4(or 5)-methylbenzoic acid (B), m.p. 227.5–228.5°[26]	2-(5′-Chloro-2′-hydroxybenzoyl)-5-methylbenzoic acid (B)

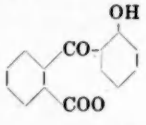
IV. **Condensation of 3-Methylphthalic Anhydride with Phenol.** When 3-methylphthalic anhydride was condensed with phenol, two hydroxybenzoyltoluic acids were obtained; one melted at 220–221° (K) and the other at 197–198° (L). When these two acids were separately treated with concentrated sulphuric acid at room temperature, an isomeric change occurred, and hydroxybenzoyltoluic acid, m.p. 141–142° (K′) from the former (K), and hydroxybenzoyltoluic acid, m.p. 183–184° (L′) from the latter (L), were produced. The four acids K, K′, L, and L′ exhibit absorption bands with heads at λ 3300 and ca. 2500, 3310 and ca. 2500, 2875, and 2880 Å, respectively.

2-(2′-Hydroxybenzoyl)-benzoic acid (XXIII)[27], m.p. 171–171.5°, and 2-(4′-hydroxybenzoyl)-benzoic acid (XXIV)[28], m.p. 212–213°, have absorption bands with heads at λ 3310 and ca. 2500, and 2880, respectively. Reasoning

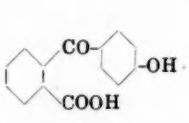
(24) *J. Chem. Soc.*, **1930**, 1518.
(25) (26) *J. Chem. Soc.*, **1930**, 1516.
(27) (28) Ullmann and Schmidt, *Ber.*, **52** (1919), 2100, 2106.

from the great similarity of these absorption bands, K or K′ should have formula XXV or XXVI which has the hydroxy-group in the *o*-position to the carbonyl-group, and L or L′ should have formula XXVII or XXVIII which has the hydroxy-group in the *p*-position to the carbonyl-group.

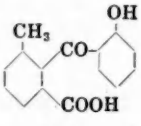
On taking into account the case of benzene, K, K′, L, and L′ would be 2-(2′-hydroxybenzoyl)-3-methylbenzoic acid (XXV), 2-(2′-hydroxybenzoyl)-6-methylbenzoic acid (XXVI), 2-(4′-hydroxybenzoyl)-3-methylbenzoic acid (XXVII) and 2-(4′-hydroxybenzoyl)-6-methylbenzoic acid (XXVIII) respectively.



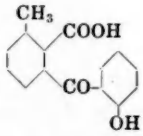
m.p. 171–171.5°
XXIII



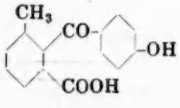
m.p. 212–213°
XXIV



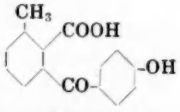
m.p. 220–221° (K)
XXV



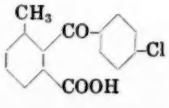
m.p. 141–142° (K′)
XXVI



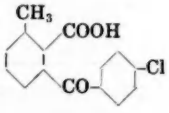
m.p. 197–198° (L)
XXVII



m.p. 183–184° (L′)
XXVIII



m.p. 175.5–176°
XXIX



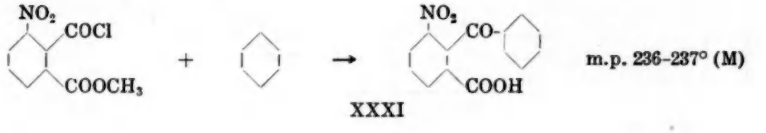
XXX

V. Condensation of 3-Methylphthalic Anhydride with Chlorobenzene. On taking into account of the general rule, chlorobenzoyltoluic acid, m.p. 175.5–176°, which was obtained by condensation of 3-methylphthalic anhydride with chlorobenzene, should have formula XXIX or XXX, and may be 2-(4′-chlorobenzoyl)-3-methylbenzoic acid (XXIX) from the analogy with the case of benzene, but an isomeric change in concentrated sulphuric acid solution was not clear.

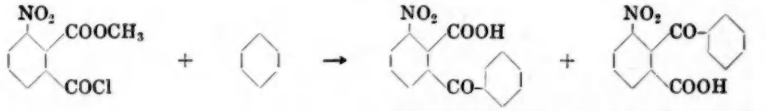
VI. Condensation of 3-Nitrophthalic Anhydride with Benzene. When 3-nitrophthalic anhydride was condensed with benzene, W. Lawrance[29] obtained two 2-benzoylnitrobenzoic acids, one melted at 217–221° and the other at 140–158–161° (decomp.) (or 157–160°), and concluded that the former is "6-benzoyl-2-nitrobenzoic acid" (XXXII) and the latter is "2-benzoyl-3-nitrobenzoic acid" (XXXI). The present authors, however, could isolate only one benzoylnitrobenzoic acid (M), m.p. 236–237°. When acid chloride of

(29) *J. Am. Chem. Soc.*, **42** (1920), 1874.

1- or 2-methyl 3-nitrophthalate was condensed with benzene[30], only isomeride M was isolated in the case of 1-methyl ester, and a small amount of isomeride M and a comparatively larger amount of isomeride N, m.p. 160–161°, in the case of 2-methyl ester. The present authors' experimental result support that isomerides M and N may be 2-benzoyl-3-nitrobenzoic acid (XXXI) and 2-benzoyl-6-nitrobenzoic acid (XXXII), respectively, not coincident with Lawrance's conclusions.



XXXI



m.p. 160–161° (N) m.p. 236–237° (M)

XXXII XXXI

On treating acid chloride of 1- or 2-methyl 3-nitrophthalate with conc. ammonia, diamide of 3-nitrophthalic acid, m.p. 204–204.5° (decomp.), was obtained in both cases[31].

Experimental.

I. **Condensation of 3-Methylphthalic Anhydride with Benzene.** Anhydrous aluminium chloride (15.4 g.) was gradually added to a solution of 3-methylphthalic anhydride (7.7 g.) in benzene (70 c.c.) with constant stirring, and then the mixture was gradually heated, boiled after 1.5 hours' heating, and maintained at a boiling state until the evolution of hydrogen chloride had almost ceased (about 2 hours). The brown coloured mass[32] was treated with aqueous sodium carbonate, a substance (10.7 g., 94%), m.p. 128–156°, was obtained from the soluble portion, and a substance (4.2 g.), m.p. 109–113°, from the insoluble portion. On fractionally crystallising the former from glacial acetic acid, two fractions were isolated. The less soluble crystals (4.3 g.) melted at 163–170° and the more soluble ones (1.1 g.) at 123–128°. The residue (4.8 g.), from which nothing definite could be isolated by further recrystallisation, melted at 100–160°.

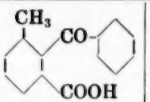
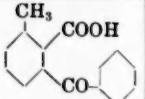
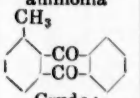
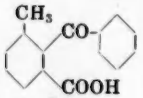
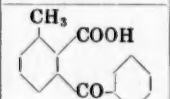
Substance A (I, II *or* III). The substance, m.p. 109–113°, crystallised from alcohol in colourless needles (Found: C, 84.26; H, 5.49; M, in camphor by Rast's method, 314, 303. Calculated for $C_{21}H_{16}O_2$: C, 83.97; H, 5.37%; M, 300.1). It melts at 116–117°, and

(30) Compare Lawrance, *ibid.*, **42** (1920), 1875.

(31) Compare p. 186, 200.

(32) From the filtrate, crude 3-methylphthalic acid (0.5 g.), m.p. 149–150° (decomp.), was recovered by extraction with ether.

Table 3.

Sample	Condition			Soluble part in ammonia					Insoluble part in ammonia
				Before recrystallisation			After recrystallisation		
					Mixed with				
	H_2SO_4 100% (c.c.)	Temp. (°C.)	Hours	m.p. (°C.)	3-isomeride m.p. (°C.)	6-isomeride m.p. (°C.)	 m.p. (°C.)	 m.p. (°C.)	 Crude: m.p. (°C.)
 0.1 g.	2	room temp.	15	155–165	164–169	—	—	—	—
0.5 g.	3	70–75	$\frac{3}{4}$	119–146 0.43 g.	145–164	113–125	157–165	?	169.5–172 0.05 g.
0.5 g.	2.5	100–105	$\frac{2}{3}$	121–125.5 0.35 g.	120–162	122–127.5	?	125.5–127 0.31 g.	167–171.5 0.1 g.
0.5 g.	2.5	100–105	$1\frac{1}{2}$	121–124° 0.23 g.	117–156	121–125.5	?		168.5–172 0.2 g.
 0.31 g.	1.6	100–105	$\frac{3}{4}$	122–125° 0.2 g.	—	122–127	—	—	168–171 0.1 g.
Residue {m.p. 100–160°, 4.8 g. m.p. 125–153°, 0.7 g.	25	100–105	$\frac{1}{2}$	110–120 4.4 g.	—	—	—	126.5–127.5 1.6 g.	— 0.83 g.

is soluble to some extent in glacial acetic acid, and appreciably in alcohol. This substance is not soluble in dilute caustic alkali, and dissolves in conc. sulphuric acid to a faintly yellow solution.

2-Benzoyl-3-methylbenzoic acid (B). When the material, m.p. 163–170°, was recrystallised several times from glacial acetic acid, fine colourless crystals, m.p. 171–172°, were obtained (Found: C, 74,85; H, 5.29. Calculated for $C_{15}H_{12}O_3$: C, 74.97; H, 5.04%). It is easily soluble in alcohol and appreciably soluble in glacial acetic acid. The solution in conc. sulphuric acid is faintly yellow. Its methyl ester melts at 106.5–107.5°.

2-Benzoyl-6-methylbenzoic acid (C). Fine colourless crystals, m.p. 126.5–127.5°, were obtained from the substance, m.p. 123–128°, by several crystallisations from glacial acetic acid (Found: C, 74.90; H, 5.43%). The solubilities of this acid are generally similar to, but greater than, those of the isomeric acid (B). Its methyl ester melts at 122.5–123°.

The results, which were obtained when 2-benzoyl-3- or 6-methylbenzoic acid was treated with conc. sulphuric acid, are given in Table 3.

Diphenylketone-2,6-dicarbonic acid (D). 2-Benzoyl-3-methylbenzoic acid (0.88 g.) was boiled with 1% potassium permanganate solution (184 c.c.) for 27 hours. The solution was concentrated and acidified with hydrochloric acid; a substance (ca. 1 g.), m.p. 249–255°, was obtained. On recrystallising from glacial acetic acid, it melted at 255–256° (Found: C, 66.60; H, 3.93. Calculated for $C_{15}H_{10}O_5$: C, 66.65; H, 3.73%).

Diphenylketone-2,3-dicarbonic acid (E). Diphenylketone-2,3-dicarbonic acid, which was obtained by oxidizing the 2-benzoyl-6-methylbenzoic acid with potassium permanganate, melted at 100–125–176–186°. It was recrystallised from acetic acid or from water; fine colourless crystals, which melted with foaming at 121–125–146°, were obtained (Found for air-dried material: loss at 100–105°/28 mm., 6.30; C, 62.53; H, 4.29. Calculated for $C_{15}H_{10}O_5.H_2O$: H_2O, 6.25; C, 62.48; H, 4.20%). Its anhydrous form melts with foaming at 140–141° (Found for anhydrous material: C, 66.73; H, 3.90. Calculated for $C_{15}H_{10}O_5$: C, 66.65; H, 3.73%).

II. **Condensation of Acid Chloride of Methyl 3- and 4-Methylphthalate with Benzene.**

(a) *Preparation of alkyl 3- and 4-methylphthalates.* As far as the authors are aware, alkyl 3- and 4-methylphthalates have not been prepared; they synthesised these esters as summarised in Table 4. These results are not in agreement with v. Meyer's theory of esterification[33].

1-Methyl 3-methylphthalate (F) (0.3 g.) was boiled with 1% potassium permanganate solution (70 c.c.) for 12 hours. The solution was concentrated and acidified with hydrochloric acid; a substance, m.p. 188–207° (decomp.), was obtained. On recrystallising from acetic acid, it melted with decomposition at 193–194° (0.15 g.).

(b) *3- and 4-Methylphthalimide.* 1-Ethyl or 1-methyl 3-methylphthalate (G or F) was boiled with thionyl chloride (5 parts) for 15–30 minutes. The excess of thionyl chloride was removed by distillation under reduced pressure. On treating the residue with an excess of conc. ammonia 3-methylphthalimide (XIV), melting at 188.5–189° after recrystallisation in both cases, was obtained (Found: N, 8.99. Calculated for $C_9H_7O_2N$: N, 8.69%).

4-Methylphthalimide (XV), which was prepared by much the same method as in the case of 3-methylphthalic acid, melted at 194.5–195° (Found: C, 67.09; H, 4.57; N, 8.92; 8.64. Calculated for $C_9H_7O_2N$: C, 67.06; H, 4.38; N, 8.69%).

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(33) *Ber.*, **27** (1897), 1585; also compare *Ber.*, **27** (1894), 510, 3146; **28** (1895), 182, 1254, 1468; **29** (1896), 1401.

Table 4.

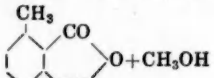
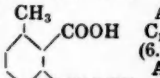
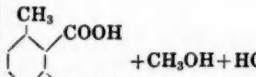
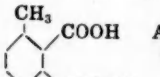
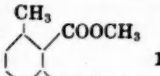
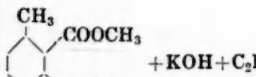
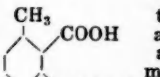
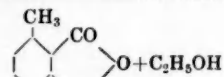
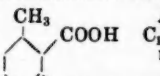
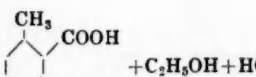
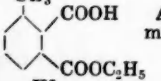
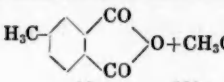
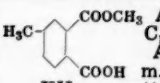
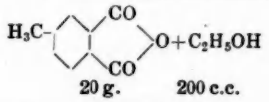
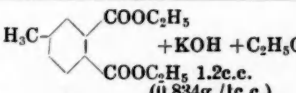
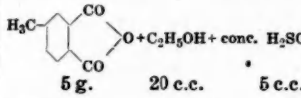
Materials	Condition	Crude product	Pure product
 19 g. 100 c.c.	boil 5 h.	Air-dried: m.p. 74–89° (22.3 g., 89.5%) Anhydrous: m.p. 109–114°	 X Air-dried: $C_{10}H_{10}O_4 \cdot H_2O$ (6.3 g., 27.7%) Anhydrous: m.p. 114.5–115° (F)
 20 g. 200 c.c.	boil ½ h.	Soluble part in Na_2CO_3: anhydrous, m.p. 101–111.5° (2.95 g., 11.3%)	 X Anhydrous: m.p. 114.5–115° (F)
		Insoluble part in Na_2CO_3: b.p. ca. 165–169°/21 mm. (15.6 g., 60.7%)	 b.p. 167–169°/21 mm.
 15 g. 5 g. 70 c.c.	boil 5 h.	Soluble part in NaOH: anhydrous, m.p. 107–112°	 Recrystallisation three times from acetic acid: anhydrous, m.p. 109–112° (3.25 g.), mixed m.p. with (F) 109–114°
 10 g. 200 c.c.	boil 2 h.	Air-dried: m.p. 71–80° (5.4 g., 38.8%) Anhydrous: m.p. 77–82°	 XI Air-dried: $C_{11}H_{12}O_4 \cdot H_2O$, m.p. 75–85° (4 g.) Anhydrous: m.p. 86–87°(G)
 4 g. 40 c.c.	boil 1 h.	Soluble part in NH_4OH: air-dried, m.p. 69–82° (0.63 g., 12%) Anhydrous: m.p. 73–83°	 XI Anhydrous: m.p. 86–87°(G)
		Insoluble part in NH_4OH	Diester
 10 g. 100 c.c.	boil 2 h.	Anhydrous: m.p. 85–90° (5.1 g., 42.6%)	 XII Air-dried: $C_{10}H_{12}O_4 \cdot H_2O$ Anhydrous: m.p. 89–90°(H) (4.7 g., 39.3%)

Table 4. (*Concluded*)

Materials	Condition	
 20 g. 200 c.c.	boil 2 h.	Pure ethyl monoester could not be isolated
 4.6 g. 30c.c.	boil 1 h.	
 5 g. 20 c.c. 5 c.c.	boil 1 h.	Diester, b.p. ca. 193–195°/27 mm. (4.6 g.)

(c) *Condensation.* When acid chloride of 1-methyl 3-methylphthalate (ca. 6 g.) was condensed with benzene (120 c.c.) in the presence of anhydrous aluminium chloride (4.5 g.), crude substance A (I, II or III)[34] (ca. 0.9 g.) and 2-benzoyl-3-methylbenzoic acid[35] (ca. 1.3 g.) were isolated but 2-benzoyl-6-methylbenzoic acid could not be separated.

Aluminium chloride (0.8 g.) was added to a solution of acid chloride of 2-methyl 4-methylphthalate (ca. 0.5 g.) and benzene (5 c.c.), and the mixture was boiled for 30 minutes. The product soluble in ammonia, on recrystallising from acetic acid, melted at 136–138° and was proved to be identical with 2-benzoyl-5-methylbenzoic acid[17].

III. An Attempt to determine the Constitutions of Benzoyltoluic Acids. (a) Preparation of methyl-2-oxo-4-(toluoxazine-3,1). *6-Methyl-2-acetoanthranil* (XVI). When 2-amino-6-methylbenzoic acid (9 g.) was boiled with acetic anhydride (50 c.c.) for one hour and distilled fractionally under reduced pressure, 6-methyl-2-acetoanthranil (7 g., 86%; b.p. 145–150°/10 mm.) was obtained. It crystallised from a mixed solvent of benzene and petroleum ether in a colourless crystalline substance, m.p. 84° (Found: C, 68.47; H, 5.40. Calculated for $C_{10}H_9O_2N$: C, 68.54; H, 5.18%).

3-Methyl-2-acetoanthranil (XVII). After a solution of 2-amino-3-methylbenzoic acid (30 g.) in acetic anhydride (150 c.c.) was boiled for one hour, some acetic anhydride was distilled and the solution cooled; 3-methyl-2-acetoanthranil (31 g., 89%), m.p. 135–136°, separated, 2 acetylamino-3-methylbenzoic acid (3 g., 7.8%), m p. 193–195° (foaming), being recovered from the filtrate on treating with water. The former was recrystallised from benzene mixed with petroleum ether, m.p. 136–137° (Found: N, 8.02%).

After recrystallisation from glacial acetic acid, 2-acetylamino-3-methylbenzoic acid melted with foaming at 196.5–197° (Found: N, 7.01. Calculated for $C_{10}H_{11}O_3N$: N, 7.25%).

5-Methyl-2-acetoanthranil (XVIII). On treating 2-amino-5-methylbenzoic acid with acetic anhydride (5 parts.), 5-methyl-2-acetoanthranil (70%, m.p. 123–124°) and 2-acetyl-

(34) See p. 191.
(35) See p. 193.

amino-5-methylbenzoic acid (30%, m.p. 177–187°) were obtained. The former crystallised from benzene in almost colourless needles (Found: N, 8.17%). The latter, on several recrystallisations from acetic acid or alcohol, showed m.p. 179–190°[36] and had no water of crystallisation (Found: N, 7.38%).

4-Methyl-2-acetoanthranil (XIX). This substance was prepared by the same method as in the above cases and melted at 102–103° (Found: N, 7.85%).

(b) **Condensation of acetoanthranil with benzene.** Acetoanthranil (50 g.) was dissolved in benzene (300 c.c.) and aluminium chloride (91 g.) gradually added with constant stirring and then the mixture boiled for 14 hours, the evolution of hydrogen chloride being very slight. The reaction mixture, after distillation in steam as usual and the addition of an excess of alkali, was extracted several times with ether, and the ethereal extract was evaporated. The resinous substance was dissolved in a small amount of alcohol, and hot dilute hydrochloric acid added; the brownish resinous substance that separated was removed. On evaporation of the alcoholic solution, a substance, m.p. 160° (decomp.), separated in 5.7% yield (5.5 g.). After the addition of alkali to the filtrate and being washed with a small amount of alcohol, substance (2 g., 3.3%, m.p. about 106°) was obtained.

2-Phenylaminodiphenylketone. After neutralisation, the former crystallised from alcohol in colourless crystals, m.p. 121.5–122° (Found: N, 5.16. Calculated for $C_{19}H_{15}ON$: N, 5.13%). It dissolves easily in ether, benzene, and glacial acetic acid. Its hydrochloride melts with decomposition at 165–167° and is hydrolysed readily in water (Found: N, 4.59. Calculated for $C_{19}H_{15}ON \cdot HCl$: N, 4.52%).

2-Aminodiphenylketone. The latter was recrystallised from alcohol; yellow long hexagonal plates, m.p. 109–110°, were obtained (Found: N, 7.08. Calculated for $C_{13}H_{11}ON$: N, 7.11%). Its hydrochloride (colourless needles) dissolves easily in water and melts with decomposition at 179–180° (Found: N, 6.07. Calculated for $C_{13}H_{11}ON \cdot HCl$: N, 5.99%).

(c) **Condensation of 3-methyl-2-acetoanthranil with benzene.** *2-Phenylamino-3-methyldiphenylketone.* 3-Methyl-2-acetoanthranil (20.3 g.) was condensed with benzene (150 c.c.) in the presence of aluminium chloride (34.1 g.), and the subsequent treatment and the separation of the reaction product were carried out as in the case of acetoanthranil. In this case, 2-phenylamino-3-methyldiphenylketone (yield as hydrochloride, 5.6 g.), m.p. 123–123.5°, was only separated (Found: N, 4.88. Calculated for $C_{20}H_{17}ON$: N, 4.88%). Its hydrochloride melts with decomposition at 166–168–173° (Found: N, 4.54. Calculated for $C_{20}H_{17}ON \cdot HCl$: N, 4.33%).

(d) **Condensation of 5-methyl-2-acetoanthranil with benzene.** 5-Methyl-2-acetoanthranil (7.3 g.), benzene (50 c.c.), and aluminium chloride (15 g.) were boiled for 22 hours with constant stirring. On treating the reaction product as in the case of acetoanthranil, crude 2-phenylamino 5-methyldiphenylketone (1.9 g., 15.9%; m.p. 159–161°), and crude 2-amino-5-methyldiphenylketone (0.1 g., 1.1%) were separated.

2-Phenylamino-5-methyldiphenylketone. It crystallised from alcohol in colourless fine needles, m.p. 163.5° (Found: C, 83.47; H, 6.26; N, 4.74. Calculated for $C_{20}H_{17}ON$: C, 83.58; H, 5.97; N, 4.88%).

2-Amino-5-methyldiphenylketone (XX). After recrystallising from alcohol, it melted at 62–63°, and was proved to be identical with Chattaway and Lewis' 2-amino-5-methyldiphenylketone[21], m.p. 64–64.5°.

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(36) Miller and Meyer, *Ber.*, **24** (1891), 1914; "Beilsteins Handbuch," 3 Ed., II, 1333: m.p. 193–194°.

(e) **The determination of constitution of 2-benzoyl-5 (or 4)-methylbenzoic acid (D)**[37]. 2-Amino-5-methyldiphenylketone, which was prepared by Chattaway and Lewis' method from *p*-toluidine and benzoyl chloride, melted at 64-64.5° (Found: N, 6.78. Calculated for $C_{14}H_{13}ON$: N, 6.58%). The diazotized solution of 2-amino-5-methyldiphenylketone (20 g.) was added to a well agitated potassium cuprous cyanide solution at 40°, the mixture was then boiled for about ten minutes, and an oily substance (α) (18 g.) was isolated by means of ether. On keeping a long time in a vacuum desiccator, a small amount of crystals, which melted at 189–190° after being recrystallised from benzene mixed with alcohol, was obtained (Found: N, 3.48. Calculated for $C_{28}H_{22}O_2N$[38]: N, 3.46%). The oily substance, filtered from these crystals was distilled several times under reduced pressure; a clear, almost colourless, viscous oil, b.p. 192–195°/19 mm., which contained no nitrogen, was obtained.

The above-mentioned substance (α) was refluxed with 20% hydrochloric acid (10 parts) for 10 hours; a sticky substance thus obtained was extracted with ether, and the ethereal solution was treated with dilute aqueous ammonia. On acidifying the ammoniacal solution with hydrochloric acid, a very small amount of crude 2-benzoyl-4-methylbenzoic acid, m.p. 144–148°, was obtained. After recrystallising from acetic acid, it melted at 149–150°, and at 149–150° or at 130–138° when it was mixed with a specimen of 2-benzoyl-5-(or 4)-methylbenzoic acid (D)[37], m.p. 150–150.5°, or of 2-benzoyl-4-(or 5)-methylbenzoic acid (E)[17], m.p. 145–145.5°. Therefore 2-methyl-5-(or 4)-methylbenzoic acid (D) should be 2-benzoyl-4-methylbenzoic acid.

Diphenylketone-2,5-dicarbonic acid, which was obtained from 2-benzoyl-4-methylbenzoic acid by oxidizing with potassium permanganate, melted at 291-292°.

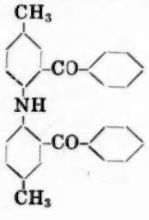
(IV) **Condensation of 3-Methylphthalic Anhydride with Phenol.** Anhydrous aluminium chloride (20 g.) was added to a solution of 3-methylphthalic anhydride (10 g.) and phenol (7 g.) in acetylene tetrachloride (50 c.c.), and the mixture was heated at 130° until the evolution of hydrogen chloride had nearly ceased (about 3.5 hours). On repeated crystallisation from glacial acetic acid, two fractions were isolated from the part solubie in aqueous sodium carbonate. One melted at 212–217° (4.5 g.) and the other at 85–101° (8 g.).

2-(2′-Hydroxybenzoyl)-3-methylbenzoic acid (K). The former crystallised from acetic acid in colourless rhombic crystals (Found: C, 70.20; H, 4.89. Calculated for $C_{15}H_{12}O_4$: C, 70.29; H, 4.72%). It melts at 220–221° and dissolves in alkali to a faintly yellow solution.

2-(4′-Hydroxybenzoyl)-3-methylbenzoic acid (L). The latter was recrystallised three times from glacial acetic acid, a substance (3.4 g.), m.p. 195–197°, being separated. On further recrystallisation from glacial acetc acid, colourless plates, m.p. 197–198°, were

(37) *J. Chem. Soc.*, **1930**, 1518.

(38)



obtained (Found: C, 70.21; H, 4.84%). It dissolves in alkali to an almost colourless solution.

2-(2′-Hydroxybenzoyl)-6-methylbenzoic acid (K′). A solution of 2-(2′-hydroxybenzoyl)-3-methylbenzoic acid (0.8 g.) in sulphuric acid (100%, 10 c.c.) was kept for 15 hours at room temperature; on pouring the product into ice-water, a precipitate (0.74 g., m.p. 122–138°) separated. It crystallised from glacial acetic acid in faintly yellow prisms (0.5 g.) (Found: C, 70.49; H, 4.97%). It melts at 141–142° and dissolves in alkali to a faintly yellow solution.

2-(4′-Hydroxybenzoyl)-6-methylbenzoic acid (L′). After a solution of 2-(4′-hydroxybenzoyl)-3-methylbenzoic acid (0.9 g.) in 100% sulphuric acid (9 c.c.) had been kept for 15 hours at room temperature, the isolated product (0.84 g., m.p. 140–146.5°) crystallised from glacial acetic acid in colourless fine crystals, m.p. 183–184° (Found: C, 70.22; H, 4.95%). It dissolves in alkali to an almost colourless solution.

(V) **Condensation of 3-Methylphthalic Anhydride with Chlorobenzene.** 3-Methylphthalic anhydride (10 g.) was condensed with chlorobenzene (50 c.c.) in the presence of anhydrous aluminium chloride (20 g.). A substance (9.2 g.), m.p. 158–162°, was obtained from the part insoluble in ammonia and chlorobenzoyltoluic acid (10 g.), m.p. 162–169°, from the part soluble in ammonia. On recrystallising the latter from glacial acetic acid, faintly yellow 2-(4′-chlorobenzoyl)-3-methylbenzoic acid was obtained (Found: C, 65.43; H, 4.22. Calculated for $C_{15}H_{11}O_3Cl$: C, 65.56; H, 4.04%). It melts at 175.5–176°.

The authors have examined the ultra-violet absorption curves of alcoholic solutions of the above-mentioned substances (Table 5).

Table 5.

Substance	Maxima of absorption bands, Å
1-Methyl-2,3-dibenzoylbenzene (A), m.p. 116–117°	2830, 2670
2-Benzoyl-3-methylbenzoic acid (B), m.p. 171–172°	2830, 2650
2-Benzoyl-6-methylbenzoic acid (C), m.p. 126.5–127.5°	2830, 2650
Diphenylketone-2,6-dicarbonic acid (D), m.p. 255–256°	2820, 2650
Diphenylketone-2,3-dicarbonic acid (E), m.p. 140–141° (foam.)	2820, 2650
1-Methyl 3-methylphthalate (F), m.p. 114.5–115°	2830, 2670
1-Ethyl 3-methylphthalate (G), m.p. 86–87°	2830, 2660
2-(2′-Hydroxybenzoyl)-3-methylbenzoic acid, m.p. 220–221° (K)	3300, ca. 2500
2-(4′-Hydroxybenzoyl)-3-methylbenzoic acid, m.p. 197–198° (L)	2875
2-(2′-Hydroxybenzoyl)-6-methylbenzoic acid, m.p. 141–142° (K′)	3310, ca. 2500
2-(4′-Hydroxybenzoyl)-6-methylbenzoic acid, m.p. 183–184° (L′)	2880
2-(2′-Hydroxybenzoyl)-benzoic acid,[27] m.p. 171–171.5°	3310, ca. 2500
2-(4′-Hydroxybenzoyl)-benzoic acid,[28] m.p. 212–213°	2880
2-(4′-Chlorobenzoyl)-3-methylbenzoic acid, m.p. 175.5–176°	ca. 2510

Table 6.

2-nitrophthalic acid monomethyl ester (g.)	Benzene (c.c.)	$AlCl_3$ (g.)	Conditions of condensation (°C.)	Conditions of condensation (hrs.)	Substance recovered from water solution. 3-nitrophthalic acid (g.)	Precipitate (g.)	Fraction soluble in ammoina (γ): 2-nitrophthalic acid monomethyl ester (g.)	Fraction soluble in ammoina (γ): 2-nitro-3-benzoylbenzoic acid	Fraction soluble in ammoina (γ): 2-nitrophthalic acid monobenzoyl ester	Fraction insoluble in ammonia (β): 2-nitro-3-benzoylbenzoic acid	Fraction insoluble in ammonia (β): 2-nitrophthalic acid monobenzoyl ester
50	250	32.5	−80 boil	5½ ½	9 g. m.p. 206–209° (decomp.)	—	2.6 g. m.p. 148–158–	0.2 g. m.p. 200–210°–	not isolated	4.6 g. m.p. 210–230°	not isolated
10	50	9	−70 boil	1 5	—	10.2	—	0.4 g. ← combined m.p. 220–224°	not isolated		not isolated
10	120	6	55–60	6	—	10.8	—	not isolated			
14	100	17	−80 boil	1 5	—	—	—	0.2 g. m.p. 229–234°	not isolated	0.15 g. m.p. 210–230°	not isolated
10	50	6	−80 boil	1 5	—	—	—	0.1 g. ← combined m.p. 200–220°	not isolated		not isolated
3-nitrophthalic acid monomethyl ester (g.)							3-nitrophthalic acid monomethyl ester				
20	200	24	−80 boil	1 4½	—	—	—	0.2 g. m.p. 228–230°	3 g.(39) m.p. 155–160°	not isolated	
50	250	32.5	−80 boil	7 ½	13.9 g. m.p. 207–215° (decomp.)	—	0.3 g. m.p. 134–140°	0.2 g. m.p. 225–230°	—	4.7 g. m.p. 223–230°	0.5 g. m.p. 148°152°
10	50	6	−80 boil	1 5	—	—	—	—	0.6 g. m.p. 146–158°	—	—

(39) On recrystallisation from glacial acetic acid, 2-benzoyl-6-nitrobenzoic acid (N) melted at 160–161° (Found: N, 5.38. Calculated for $C_{14}H_9O_5N$: N, 5.17%).

(VI) Condensation of 3-Nitrophthalic Anhydride with Benzene. 3-Nitrophthalic anhydride (50 g.) was dissolved in benzene (300 c.c.), aluminium chloride (75 g.) was added with constant stirring, and the mixture heated slowly and boiled in the course of 40 minutes. After 5 hours' boiling, the product was mixed with ice-water and, after the addition of hydrochloric acid (90 c.c.), distilled in steam. The residue was extracted with aqueous ammonia, the ammoniacal extracts were freed from ammonia, cooled, and the resinous substance that separated was removed. On acidification of the filtrate, a sticky precipitate (27.3 g.) separated. This substance was dissolved in glacial acetic acid and treated with animal charcoal, the substance (2 g.), m.p. 220–228°, thus obtained was recrystallised from glacial acetic acid; faintly yellow rhombic crystals (Found N, 5.27. Calculated for $C_{14}H_9O_5N$: N, 5.17%). 2-Benzoyl-3-nitrobenzoic acid (M) melts at 236–237°. When this acid was heated with 100% sulphuric acid (10 parts) at 100–105° for 45 minutes or kept for 17 hours at room temperature, no isomeric change occurred.

Condensation of acid chloride of 1- or 2-methyl 3-nitrophthalate with benzene. To a solution of acid chloride of 1- or 2-methyl 3-nitrophthalate in benzene, aluminium chloride was added, and the mixture boiled. On treating the product as usual, an insoluble part (β) in ammonia and an ammoniacal solution (γ) were obtained. The latter (γ) was boiled with animal charcoal, and acidified with hydrochloric acid; the resinous substance thus precipitated was recrystallised fractionally from acetic acid or purified by preparing its barium salt. The former (β) was extracted several times with boiling alcohol, and the alcoholic solution was boiled with 50% KOH solution. The fraction soluble in alkali was recrystallised fractionally from acetic acid. Their results are given in Table 6.

Diamide of 3-nitrophthalic acid. On treating acid chloride of 1-methyl 3-nitrophthalate (m p. 97.5–99.5°)[40] or 2-methyl 3-nitrophthalate (m.p. 95–97°)[41] with an excess of conc. ammonia and recrystallising from alcohol, colourless fine crystals were obtained in each case (Found: N, 20.21. Calculated for $C_8H_7O_4N_3$: N, 20.10%). They melt with decomposition at 204–204.5°[42].

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(40) *J. Chem. Soc.*, **109** (1916), 234: m.p. 97–99°.
(41) *J. Chem. Soc.*, **109** (1916), 234: m.p. 95–97°.
(42) *J. Am. Chem. Soc.*, **23** (1901), 747: m.p. 200–201° (decomp.).

ON THE DERIVATIVES OF ANTHRAHYDROQUINONE DISULPHURIC ACID ESTERS. I. SYNTHESIS OF SOME AZO-COMPOUNDS.

By Kenji IWAMOTO.

Received November 2nd, 1935. Published March 28th, 1936.

Bader and Vaucher[1] synthesised leuco-indigo disulphuric acid ester treating indigo white with pyridine salt of chlorosulphonic acid. Its alkali salt is stable and highly soluble in water. In acid solution, however, indigo is easily precipitated by the action of weak oxidising agents such as ferric chloride or sodium nitrite, due to the hydrolysis and oxidation taking place simultaneously. Inasmuch as fabrics may be dyed with indigo without the use of alkali, of the so-called Indigosol dyes belonging to this class, many are actually prepared. Schirmacher, Scharich, and Eishold[2] synthesised the anthrahydroquinone disulphuric acid ester or its derivatives, by mixing anthraquinone or its derivatives with pyridine salt of chlorosulphonic acid, then reducing and esterifying the mixture by means of metallic powder. Moreover the fact that these compounds are soluble in water and easily oxidisable to the original quinone in acid solution has been utilized in many attempts in the field of dye-synthesis[3]. The present author synthesised the same compound and examined the properties.

Sodium salt of anthrahydroquinone disulphuric acid ester was readily prepared as yellow crystals by the method of German patent 473 471. But the isolation of alkali or alkaline earth salts of β-aminoanthrahydroquinone disuphuric acid ester proved unsuccessful owing to the great solubilities of salts. After many experiments, the author succeeded in isolating it in the form of diphenylguanidine salt. The latter is difficultly soluble in water, and may be purified by recrystallisation from alcohol in yellow crystals. On adding alkali, it is converted into the sodium salt, and free diphenylguanidine formed is removed by filtration.

Next, using this compound, the author synthesised some azo-dyes. The diazo-compound is readily prepared by the usual method as the compound is easily soluble in water. By coupling with α- and β-naphthol, dark, violet

(1) *Chimie & Industrie*, **1924**, 449.
(2) D. R. P. 473471.
(3) D. R. P. 461500, 472772, 470809, 476811.
E. P. 333506, 333507, 338891.

powders were obtained which dyed animal fibres in good colour in weak acid baths.

These dyed fabrics were reddish-violet and changed into scarlet by the action of hot ferric chloride solution. Dye from β-naphthol was pure scarlet.

Dye from α-naphthylamine was reddish-orange in alkaline solution and dyed the fibres scarlet. This turned bluish-violet with acid and again violet-red on oxidation. β-Naphthylamine derivative was also orange-red in alkaline solution and dyed the fibre reddish, which turned violet-red by the action of ferric chloride. But its shade did not come out as clear as in the case of α-derivative.

Experimental.

Sodium Salt of Anthrahydroquinone Disulphuric Acid Ester, $C_6H_4(COSO_3Na)_2C_6H_4$. Chlorosulphonic acid (8 g.) was slowly poured into pyridine (50 c.c.) cooled with ice. The mixture was then heated to 30°, anthraquinone (5 g.) was introduced in and the whole was heated to 65°. Copper powder ("Naturkupfer C") was then added in small quantities at a time with constant stirring, the temperature was raised to 70° and maintained for half an hour. After cooling, sodium hydroxide solution (10 g. NaOH) was poured in, pyridine was distilled over with steam, and the solution was filtered while hot. The filtrate was evaporated on the water-bath. On cooling, anthrahydroquinone disulphuric acid ester disodium salt was crystallised out. The yield of the crude product was 10.5 g. After two crystallisations from water, it separated in faintly yellow crystals. The solution showed violet fluorescence and anthraquinone was precipitated on treating the solution with ferric chloride. The solid salt is also unstable and decomposes into anthraquinone when it is kept in a bottle for some days or more rapidly when it is hot. In the above case, reduced iron powder or bronze powder was used as the reducing agent, but the treatment was not found effective.

Diphenylguanidine Salt of β-Aminoanthrahydroquinone Disulphuric Acid Ester, $C_6H_4(COSO_3H\cdot C_{13}H_{11}N_3)_2C_6H_3NH_2$. To well-cooled pyridine (200 c.c.) chlorosulphonic acid (48 c.c.) was added drop by drop with vigorous stirring, keeping the temperature below 5°. The salt thus obtained was warmed to 40°, β-acetaminoanthraquinone (26.5 g.) was introduced to the solution and the mixture was heated to 65°. To this suspended mixture, copper powder ("Naturkupfer C," 30 g.) was added gradually with constant stirring, while the temperature was maintained at 70° for an hour. At first the suspension was dissolved in yellow solution, and in a short time the whole was again crystallised to form a paste. After leaving overnight, the product was heated to 40° with stirring, and sodium hydroxide solution (90 g. NaOH in 300 c.c. of water) was slowly poured in until the product was dissolved. From the solution pyridine was removed by steam distillation and the copper salt was filtered off. The filtrate was cooled, 40 c.c. of hydrochloric acid was added and the brown precipitate was again removed by filtration. The solution was then neutralised with sodium bicarbonate and 400 c.c. of diphenylguanidine hydrochloride [$C_6H_5NH\cdot C(:NH)\cdot NHC_6H_5\cdot HCl$] solution (10%) was poured in, when brown precipitate was deposited. The precipitate was collected, washed with water, and dried. Recrystallised three times from alcohol, lemon-yellow crystals were obtained. The yield was 65.5 g. after one crystallisation, 80% of the theoretical. The salt was dissolved in

hydrochloric acid and treated with ferric chloride while hot. Orange crystalline aminoanthraquinone was deposited (0.4681 g. of the salt gave 0.1294 g. aminoanthraquinone. Found : 27.94. Calculated : 27.64%).

The sodium salt was obtained as a solution by treating the diphenylguanidine salt with sodium hydroxide and filtering it. The solution was brownish-yellow with strong, green fluorescence.

Sodium Salt of Leuco-β-anthraquinone-azo-α-naphthol Disulphuric Acid Ester, $C_6H_4(COSO_3Na)_2C_6H_3N{:}NC_{10}H_6OH(4)$. Aminoanthrahydroquinone sulphuric acid ester diphenylguanidine salt (8.1 g., 1/100 mol) was changed into sodium salt by treating with caustic soda solution (3 g. NaOH in 30 c.c. of water), filtering, and washing with water. The yellow solution (80 c.c.) was then cooled to 0°, 10 c.c. of hydrochloric acid was added and diazotised by dropping sodium nitrite solution (0.69 g. in 7 c.c. of water). The diazo-compound was not easily soluble in water and formed carmine-red precipitate. α-Naphthol (1.45 g., 1/100 mol) with sodium hydroxide (4 g.) was dissolved in 80 c.c. of water, and to this cold solution the above diazo-solution was poured in as a thin stream with constant stirring. A violet solution obtained was stirred for two hours more and heated to 80° for an hour. This was filtered and salted out with sodium chloride and sodium bicarbonate. The dark-violet, amorphous powder was collected, washed with salt solution, and dried. It gave a deep-reddish-violet solution and dyed the animal fibre violet-red in a weak acid-bath. This colour of the dyed fabrics may be changed red by oxidation with hot ferric chloride and hydrochloric acid, but the colour shade of this changed dye is not so fine as that of the β-isomer.

Sodium Salt of Leuco-β-anthraquinone-azo-β-naphthol Disulphuric Acid Ester, $C_6H_4(COSO_3Na)_2C_6H_3N{:}NC_{10}H_6OH(2)$. Diazotisation and coupling were carried out similarly to the above case. On salting out the dye with sodium chloride, violet precipitate was formed. This was collected, washed with salt solution, and dried. It was very soluble in water and produced a violet-red solution. Silk was dyed violet-red from its weak acid-bath, the colour was changed into bright-scarlet when oxidised with ferric chloride solution. The solution also gives a scarlet precipitate by the action of ferric chloride. The latter was recrystallised from tetraline, from which it separated in scarlet needles, m.p. 262°. The product thus obtained is β-anthraquinone-azo-β-naphthol. Kaufler[4] and Maki[5] synthesised the same substance from β-diazoanthraquinone and β-naphthol, and gave m.p. 262°.

Sodium Salt of Leuco-β-anthraquinone-azo-α-naphthylamine Disulphuric Acid Ester, $C_6H_4(COSO_3Na)_2C_6H_3N{:}NC_{10}H_6NH_2(4)$. Diphenylguanidine salt (8.1 g., 1/100 mol) was treated with sodium hydroxide solution and the solution of sodium salt (80 c.c.) was acidified with 10 c.c. of hydrochloric acid. This was cooled well and diazotised with sodium nitrite solution until the reaction was complete when tested with potassium-iodide-starch-paper. α-Naphthylamine (1.43 g., 1/100 mol) was dissolved in hot solution of hydrochloric acid (3 c.c. in 80 c.c. of water) and cooled rapidly. To this suspension of hydrochloride, the above diazo-solution was poured in and the sodium acetate solution (20 g. in 30 c.c. of water) was added gradually with vigorous mixing. The stirring was continued for 3 hours and the mixture became brownish. On standing overnight, it was heated to 80° for an hour and made alkaline with sodium hydroxide solution. From the filtered solution, a brownish-red precipitate was produced by salting out with sodium

(4) *Chem. Zentr.*, **1904**, I, 289.
(5) *J. Soc. Chem. Ind., Japan*, **32** (1929), 348 B.

chloride. This was collected and washed with sodium chloride solution. This substance is brownish-red in aqueous solution but in acid solution the colour changed to violet, and dyed the animal fibre deep-violet in weak acid-bath. It was changed reddish-violet by the action of oxidising agent.

Potassium Salt of Leuco-β-anthraquinone-azo-β-naphthylamine Disulphuric Acid Ester, $C_6H_4(COSO_3K)_2C_6H_3N{:}NC_{10}H_6NH_2$(2). This dye was synthesised similarly to the above case. As its sodium salt was very viscid, the coupled solution was made alkaline with potassium hydroxide when a deep-scarlet solution was obtained. It was filtered and salted out with potassium chloride as brownish-red powder, which was collected and washed with a solution of the same salt. It dyes the fibre orange-red and turns violet-red by oxidation. Its shade is somewhat not clear.

In conclusion, the author wishes to express his gratitude to Prof. R. Majima for his valuable suggestions, also to Dr. T. Ogata and Dr. M. Nakanishi for their kind advices. Moreover, the author's appreciation is expressed to the Nippon Gakujutu-Sinkokai for a grant toward this research.

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ÜBER DIE KATALYTISCHE HYDRIERUNG VON ROHRZUCKER. I. HYDRIERUNG VON ROHRZUCKER MIT REDUZIERTEM NICKEL ALS KATALYSATOR.

Von **Tsuneharu TANNO.**

Eingegangen am 2. November 1935. Ausgegeben am 28. März 1936.

Der Zweck dieser Untersuchung war darauf gerichtet, dass die Einwirkung von Hochdruck-Wasserstoff auf dem Rohrzucker selbst [ohne Inversion, d.h. das den Brückensauerstoff enthaltende Rohrzuckermolekül oder *α-d*-Glukopyranosido-*d*-Fruktofuranosid], in Gegenwartt von Katalysator, festgestellt würde. Dabei wurden die Bedingungen, die Mechanismen und die Produkten der Reaktion von Wasserstoff auf dem Rohrzuckern versucht. Als Katalysator wurde erst das reduzierte Nickel genommen.

Die Berichte über die katalytische Hydrierung der Disaccharide bei den hohen Temperaturen und Drucken werden erst von Ipatiew[1] und in dieser Zeit von Adkins[2] und Yoshikawa[3], ausser einigen Patentbeschreibungen[4],

(1) Wl. Ipatiew, *Ber.*, **45** (1912), 3226.
(2) H. Adkins u. W. H. Zartmann, *J. Am. Chem. Soc.*, **55** (1933), 4559.
(3) K. Yoshikawa, *Bull. Inst. Phys. Chem. Research, Japan*, **13** (1934), 1045. J.P. 106376 (1934).
(4) C.C. Fowler, U.S.P. 1493623 (1924). I.G. Farbenind, A-G., D.R.P. 541326 (1927); E.P. 299373 (1928); F.P. 622873 (1928).

nur bekannt gemacht. Der Bericht von Adkins und der von Yoshikawa sind im Laufe dieser Arbeit in die Öffentlichkeit gegangen.

Hier berichte ich nur kurz über die Hauptpunkte dieser Versuche und möchte in späteren Zeiten im Detail erklären.

I. Die Wirkung des Hochdruck-Wasserstoffs gegen den Rohrzuckern. Der Rohrzucker unter Suspendierung in Dekalin wurde mit dem reduzierten Nickel-Katalysator und etwa 100 Atm. Wasserstoff im Autoklav erhitzt, da zeigt es sich, dass die Wirkung des Wasserstoffs gegen den Rohrzuckern, sich in zwei Stufen teilend, sich entwickelt. Nämlich die Wirkung in erster Stufe verläuft bei 155–175° verhältnismässig schnell und ging zum Reaktionsende in einigen Stunden (erste Reaktion), die in zweiter Stufe verläuft bei etwa 225° auffallend langsam und endet nach 20 Stunden (zweite Reaktion).

II. Die erste Reaktion und die Reaktionsprodukte. Bei der ersten Reaktion gibt es zwei Reaktionsfälle. In einem Falle nimmt ein Rohrzuckermolekül etwa drei Wasserstoffmolekülen bei 170–175° bis zum Ende der Reaktion (Reaktion-A), in anderem Falle nimmt es bei 155–160° etwa zwei Wasserstoffmolekülen bis zum Ende der Reaktion (Reaktion-B).

In beiden Reaktionsfällen verändert sich das Anfangsmaterial (Rohrzucker) so genau dass fast kein Rohrzucker so wie reduzierender Zucker im Reaktionsprodukte gefunden werden.

Aus dem Produkte der Reaktion-A oder -B wurden *d*-Mannit und *d*-Sorbit in der gleichen Menge erhalten und die Gesamtmenge dieser beiden Hexiten entsprach der Hälfte des gebrauchten Rohrzuckers.

Aus dem Produkte der Reaktion-A wurde ein neues Methylpentit[5] d.i. *l*-Gulomethylit, $C_6H_{14}O_5$, Siedp. 182–183°, $[\alpha]_D^{22} = +2.04$ (in Wasser, 2.46%) gefunden.

Bei der Reaktion-B bildet sich kein *l*-Gulomethylit und nach der Abscheidung des Mannits und Sorbits von dem Reaktionsprodukte bleibt eine harzige Substanz hinter, welche schon unter den Bedingungen der Reaktion-B nicht mit Wasserstoff wirksam ist, aber unter den Bedingungen der Reaktion-A durch zweimalige Wirkung von Wasserstoff *l*-Gulomethylit gibt.

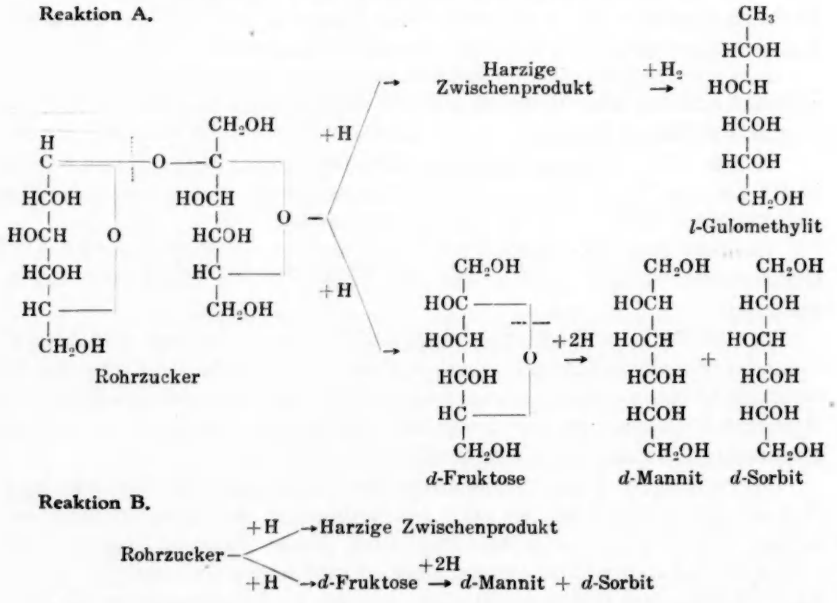
Wenn man den Fruchtzucker unter den Bedingungen der Reaktion-A mit Wasserstoff wirken lässt, so geht die Hydrierung des Fruchtzuckers sehr schnell vonstatten und aus den Produkten dieser Reaktion werden leicht *d*-Mannit und *d*-Sorbit gewonnen, aber es gibt kein *l*-Gulomethylit. Dabei zeigt es sich, dass Gulomethylit nicht aus den Fruktosidradikalen des Rohrzuckermoleküls, sondern aus dem Glukosidradikalen hergestellt worden ist.

(5) E. Votoček u. F. Valentin, *Bull. soc. chim.*, **43** (1928), 216; E. Votoček u. J. Mikšič, *ibid.*, **43** (1928), 220; E. Votoček u. F. Valentin, *Collect. trav. chim. Tchéco.*, **2** (1930), 36; E. Votoček u. V. Kučerenko, *ibid.*, **2** (1930), 47.

Mit anderen Worten, bei der Reaktion-A wirkt ein Rohrzuckermolekül mit etwa drei Wasserstoffmolekülen und dabei werden die gleiche Mengen von *d*-Mannit und *d*-Sorbit (jeder, dem Vierteln der gebrauchten Zuckermengen entsprechend) und *l*-Gulomethylit hergestellt. Aber bei der Reaktion-B, wirkt ein Rohrzuckermolekül mit etwa zwei Wasserstoffmolekülen und dabei entstehen die gleiche Mengen von *d*-Mannit und *d*-Sorbit, wie bei der Reaktion-A, und ein Zwischenprodukt welche unter den Bedingungen von Reaktion-A wieder mit Wasserstoff wirkend *l*-Gulomethylit erzeugen kann.

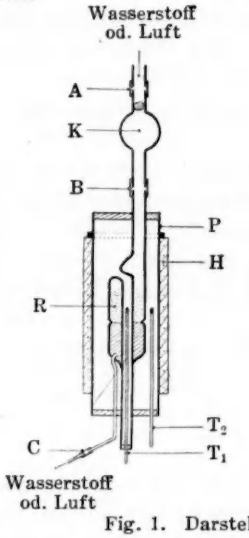
III. Mechanismus der ersten Reaktion. Von hier gewonnene Experimentsresultäte zeigt es sich, dass der Mechanismus der ersten Reaktion, bei der hydrogenolytische Hydrierung des Rohrzuckers in Anwesenheit von reduzierten Nickel-Katalysator unter der hohen Temperatur und Wasserstoffdrucken, ist wie folgend (Diagramm 1.):

Diagramm 1. Mechanismus der ersten Reaktion.



Diese Resultäte zeigen auch, dass die Hydrierung des Rohrzuckers, wie die Fälle seiner Hydrolyse erst an dem Brückensauerstoff und dann an dem Furanring und Pyranring stattgefunden werden, und vielleicht, dass der Furanring leichter als Pyranring gespaltet wird.

IV. Darstellung des Katalysators. Da die Herstellungsverfahren des reduzierte Nickel-Katalysators auf seiner Fähigkeit charakteristischen Einfluss ausübt, es wird in besonderem Darstellungsvorrichtung (Fig. 1) vorsichtig hergestellt, um den Katalysator möglichst von einheitlichen Fähigkeiten zu gewinnen.



H: Elektrischer Ofen.
P: Glaszylinder (Pyrex).
K: Kugel, in welche reduzierter Katalysator eingetragen wird.
R: Oxydations- und Reduktionsraum des Katalysators.
T_1, T_2: Thermometer.

Fig. 1. Darstellungsvorrichtung des Katalysators.

Diese Vorrichtung ist dadurch gekennzeichnet, dass der Katalysator bei der einheitlichen Temperatur oxydiert und reduziert werden kann und der reduzierte Katalysator ohne Berührung nach die Luft und verhältnissmässig einfach in Gebrauch gebracht werden kann.

Katalysatorpulver, welche in den Räumen R reduziert worden ist, wird in die Kugel K eingetragen und dann wird sie an beiden Enden (A und B) geschmolzend eingeschlossen. Auf dieser Weise wird der in Glaskugel eingeschlossene, reduzierte Nickel-Katalysator fertiggemacht.

Zum Schluss möchte ich Herrn Prof. Dr. R. Majima für die freundlichen Ratschläge und Herrn T. Hara für die eifrigen Hilfen meinen herzlichsten Dank aussprechen.

Institut der Physikalische und Chemische Untersuchung, Tokio.

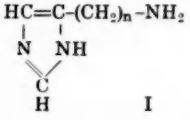
Ammerkung am 17. Februar: Nach nochmaligen Versuche wurde festgestellt dass die als *l*-Gulomethylit betrachtete Flüssigkeit ein Gemisch von Propylenglykol und Glycerin ist.

SYNTHESE VON IMIDAZOLDERIVATEN AUS α-AMINOSÄUREN. III. SYNTHESE VON ZWEI HÖHEREN HOMOLOGEN DES HISTAMINS.[1]

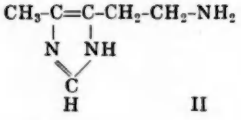
Von Shiro AKABORI und Takeo KANEKO.

Eingegangen am 4. November 1935. Ausgegeben am 28. März 1936.

Seitdem es bekannt geworden ist, dass Histamin (bei I n = 2) beträchtliche physiologische Wirkungen ausübt, wurden dessen verschiedene Derivate und Homologe auf synthetischen Wege dargestellt. Davon hat das von Ewins[2] gewonnene 5-Methyl-histamin (II) etwas ähnliche physiologische Wirkungen wie Histamin, während die andern weitaus schwächere Wirkungen haben.

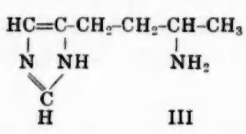


I



II

Wie man aus den Literaturen ersieht, verändern sich wahrscheinlich seine physiologischen Wirkungen merklich, wenn man seine Struktur nur ein wenig verändert. Wir glauben, es würde interessant sein, weiter zu forschen, in welcher Beziehung die Grösse von n in 4-(ω-Aminoalkyl)-imidazol, die die allgemeine Formel wie I hat, zu der physiologischen Wirkung steht. Von solchen Imidazolderivaten ist nur Imidazolyl-methylamin (bei I n = 1) bekannt; die Verbindungen mit n von mehr als 3 sind noch nicht zur Synthese gekommen.



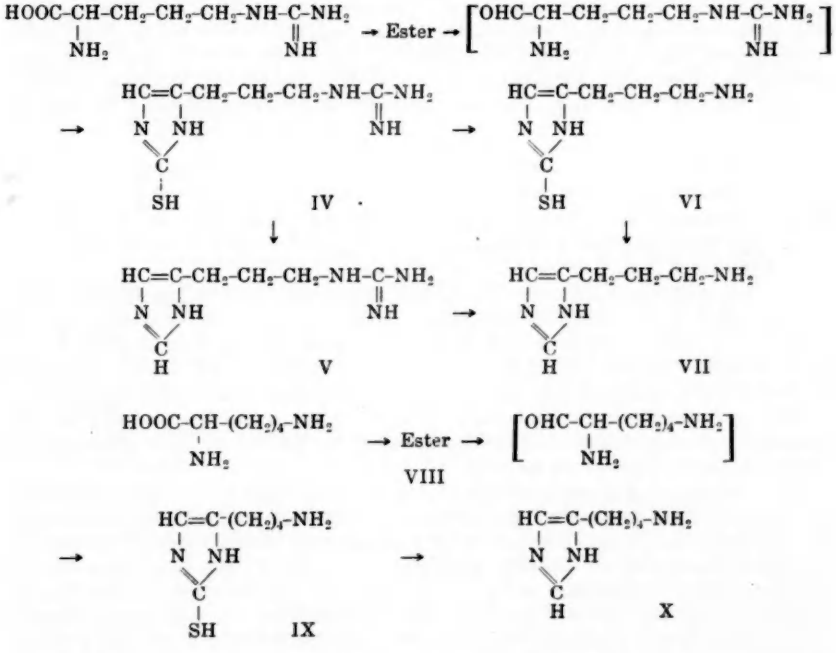
III

Pyman[3] wollte die physiologische Wirkung von Imidazolyl-propylamin (bei I n = 3) kennen lernen, aber da die Synthese dieser Verbindung Schwierigkeit bietet, bereitete er ihr Methylderivat, nähmlich 1-Imidazoly-3-aminobutan (III). Diese Verbindung dürfte aber zum Vergleich mit Histamin ungeeignet sein, da seine Aminogruppe an sekundären Kohlenstoff gebunden ist.

Nach Pyman[3] haben sowohl Imidazolyl-methylamin als auch 1-Imidazolyl-3-aminobutan eine viel schwächere Wirkung (Erregungswirkung auf glatte

(1) II. Mitt., *Ber.*, **66** (1933), 159.
(2) *J. Chem. Soc.*, **99** (1911), 2052.
(3) *J. Chem. Soc.*, **111** (1917), 1125. van der Merwe, *Z. physiol. Chem.*, **117** (1928), 301.

Muskeln) als Histamin. Es ist aber oft zu beobachten, dass, wenn man in den Verbindungen, die eine kettenförmige Atomgruppe haben, die Atomzahl der Kette sukzessiv vermehrt, verschiedene Eigenschaften der Verbindungen um je ein Atom, steigend und fallend, periodisch verändert werden. Auch im bezug auf die Verbindungen, die eine allgemeine Formel wie I haben, ohne Rücksicht auf die Wirkungen aller Fälle, wo n 1–4 beträgt, wird man deshalb über die Beziehung der chemischen Konstitution zu den physiologischen Wirkungen keinen endgültigen Schluss ziehen können. Deshalb versuchten wir γ-Imidazolyl-propylamin (bei I n = 3) und δ-Imidazolyl-butylamin (bei I n = 4) synthetisch darzustellen und ihre physiologischen Wirkungen mit denen des Histamins zu vergleichen. Zur Synthese wandten wir die in I. und II. Mitteilungen[4] beschriebenen Methoden auf Arginin und Lysin an und konnten auf folgendem Wege zum Ziele gelangen.



Bezüglich VII und X versuchten wir ihre Wirkung auf den Uterus und Darm eines nicht schwangeren Kaninchens festzustellen. Dabei zeigte das

(4) *Ber.*, **66** (1933), 153, 159.

erstere eine ziemlich starke Erregungswirkung, die aber schwächer als die des Histamins ist, und das andere nur eine äusserst schwache. (Diese physiologische Untersuchung wurde von Dr. T. Takase, dem Dozent im pharmakologischen Institut der Kaiserlichen Universität zu Sendai vorgenommen. An dieser Stelle sagen wir ihm für seine Güte unseren besten Dank.)

Wegen geringeren Probestoffes konnten wir keinen genauen Versuch machen, aber es ist wohl sicher, dass sich die eigentümliche starke Erregungswirkung von Histamin auf glatte Muskeln dann plötzlich vermindert, wenn n in Formel I auf 1 abnimmt oder auf mehr als 3 zunimmt, nicht aber periodisch verändert.

Experimenteller Teil.

Arginin-äthylester-dichlorhydrat. Das durch Zersetzung von 29.5 g. Arginin-flavianat durch Salzsäure erhaltene sirupöse Arginin-dichlorhydrat wird mit 350 c.c. 3.5% Chlorwasserstoff enthaltenem absolutem Alkohol 3.5 Stunden gekocht, 70 c.c. Benzol hinzugefügt, erst unter normalen Druck destilliert, bis Benzol fast abdestilliert ist, und dann unter vermindertem Druck zum Sirup konzentriert. Das so erhaltene Arginin-äthylester-dichlorhydrat kann man nicht kristallinisch erhalten. Deshalb löst man es in absolutem Alkohol, bis das Volum von 45 c.c. hat und gebraucht davon je 15 c.c. für folgende Versuche.

2-Mercapto-4-(ω-guanidinopropyl)-imidazol (IV). 15 c.c. alkoholische Lösung von Arginin-äthylester-dichlorhydrat (entsprechen 3.5 g. Arginin) wird in 25 c.c. kaltem Wasser gelöst, durch Kältemischung auf −12 bis −17° abgekühlt, unter tüchtigem Rühren 120 g. 2.3% Natriumamalgam langsam eingeworfen, während 23 c.c. 5N Salzsäure dazu getröpfelt wird, um die Lösung sauer zu halten.

Die Reaktionsflüssigkeit wird von Quecksilber getrennt, filtriert, unterhalb 50° unter vermindertem Druck destilliert und solange konzentriert, bis das Kochsalz sich auszuscheiden beginnt. 4.5 g. Ammoniumrhodanid wird dazu gefügt, und auf dem Wasserbad zur Trockne eingedampft. Wird der Rückstand mit 100 c.c. absolutem Alkohol gekocht, unlösliche Substanz abfiltriert und aus dem Filtrat Alkohol abdestilliert, so bleibt eine sirupöse Substanz zurück. Wird sie in ein wenig Wasser gelöst und eine gesättigte wässerige Lösung von Quecksilberchlorid im Überschuss zugefügt, so scheidet sich ein harziger Niederschlag aus.

Der Niederschlag wird in heissem Alkohol gelöst, nach gewöhnlicher Weise mit Schwefelwasserstoff zersetzt, von Quecksilbersulfid abfiltriert und das Filtrat eingedampft. Die zurückbleibende sirupöse Substanz wird im warmen Butylalkohol gelöst und von unlöslicher anorganischer Substanz abfiltriert. Wird das Filtrat unter vermindertem Druck zum Sirup konzentriert und stehen gelassen, so scheiden sich hellgelbe sandige Kristalle (0.7 g.) aus, die bei 218–223° unter Aufschäumen und Bräunung schmelzen. Das aus Essigsäure zweimal umkristallisierte farblose Produkt beginnt sich bei ungefähr 220° zu bräunen, schmilzt bei 235.5–237.5° unter Aufschäumen und wird nach beendetem Aufschäumen zu einer braunen durchsichtigen Flüssigkeit (Gef.: N, 27.72, 28.34; Cl, 14.10; S, 13.12. Ber. für $C_7H_{13}N_5S$·HCl: N, 29.72; Cl, 15.04; S, 13.61%).

Die Analysenwerte sind etwas niedriger, als man sie für $C_7H_{13}N_5S$·HCl berechnete, aber die Huntersche Farbenreaktion für 2-Mercaptoimidazol ist stark positiv und es

entwickelt sich Ammoniak wenn man es mit Bariumhydroxyd kocht. Daraus kann man die erhaltene Substanz wohl als die gewünschte ansehen.

γ-Imidazolyl-propyl-guanidin (V). 0.3 g. Hydrochlorid von IV wird in 10 c.c. Wasser gelöst, dazu 2 g. Eisenchlorid in 10 c.c. Wasser hinzugefügt, das ganze auf dem Wasserbad 1 Stunde erhitzt und mit 20 g. Phosphorwolframsäure in 20 c.c. Wasser versetzt, wobei sich ein weisser feinpulveriger Niederschlag ausscheidet.

Da die Filtration schwierig ist, wird der Niederschlag durch Zentrifugieren getrennt, mit 5% Schwefelsäure gewaschen, wiederum durch Zentrifugieren getrennt, dann mit 10 g. Bariumhydroxyd in Mörser gut verrieben und nach Zusatz von Wasser filtriert. Wird in das Filtrat genügend Kohlensäure eingeleitet, Bariumcarbonat abfiltriert und das Filtrat auf dem Wasserbad konzentriert, so bleibt eine starke alkalische Substanz zurück. Wird diese in ein wenig Wasser gelöst, 0.7 c.c. 5 N Salpetersäure hinzugefügt und das ganze mit Eis gekühlt, so scheidet sich Imidazolyl-propyl-guanidin-dinitrat in weissen Kristallen aus. Zur Reinigung kristallisiert man sie aus Wasser zweimal um. Schmp. 183.5–184° (Bräunung und Aufschäumen). Die Analysenwerte stimmen mit Imidazolyl-propyl-guanidin-dinitrat überein (Gef.: N, 33.68. Ber. für $C_7H_{13}N_5 \cdot 2HNO_3$: N, 33.45%).

Wird zur Mutterlauge obiges Dinitrats eine Lösung von 0.4 g. Pikrinsäure in 100 c.c. heissem Wasser hinzugefügt, so scheiden sich gelbe Kristalle aus (0.1 g.). Aus Wasser umkristallisierte Kristalle schmelzen bei 258° unter Zersetzung. Das Flavianat stellt in Wasser schwerlösliche orangerote Kristalle dar, die bei 248° unter Zersetzung schmelzen.

γ-Imidazolyl-propylamin (VII). Zu Überführung von 2-Mercapto-4-(ω-guanidino-propyl)-imidazol (IV) in 2-Mercapto-imidazolyl-propylamin (VI) wird 0.2 g. Chlorhydrat des ersten mit einer Lösung von 0.8 g. kristallinischen Bariumhydroxyd in 20 c.c. Wasser versetzt, nach mehrstündigen Kochen Kohlensäure eingeleitet, Bariumcarbonat abfiltriert und das Filtrat zur Trockne eingedampft, wobei eine geringe Menge sirupöse Substanz zurückbleibt. Wird eine kleine Menge davon ins Reagenz-glas genommen und der Hunterschen Reaktion unterworfen, so wird eine tiefrote Farbe erzeugt. Durch diese Farbenreaktion lässt sich vermuten, dass ein Teil des Mercapto-imidazolylderivats schon seine Mercaptogruppe verlor. Wir verzichteten darauf, 2-Mercapto-imidazolylpropylamin zu isolieren.

Die sirupöse Substanz wird in ein wenig Wasser gelöst, eine Lösung von 1.4 g. Eisenchlorid in 5 c.c. Wasser hinzugefügt, eine Stunde auf dem Wasserbad erhitzt und dann 50% Lösung von Phosphorwolframsäure hinzugefügt, wobei sich ein weisser Niederschlag ausscheidet. Dieser wird abfiltriert, mit 5% Schwefelsäure gewaschen, mit einer Lösung von 2 g. Bariumhydroxyd in 10 c.c. Wasser versetzt und nach kurzem Kochen filtriert. Das Filtrat wird durch Einleiten von Kohlensäure von Ba befreit, auf dem Wasserbad konzentriert, eine Lösung von 0.5 g. Pikrinsäure in 20 c.c. heissem Wasser hinzugefügt, wobei sich gelbe Kristalle in Nadeln ausscheiden, Ausbeute 0.2 g., 95% der Theorie. Die erst aus Alkohol und dann aus Wasser umkristallisierte Kristalle schmelzen bei 244–244.5° (unter Bräunung und Aufschäumen). Die Analysenwerte stimmen mit Imidazolyl-propylamin-dipikrat $C_6H_{11}N_3 \cdot 2C_6H_3O_7N_3$ überein (Gef.: C, 37.39; H, 3.20; N, 21.58. Ber. für $C_6H_{11}N_3 \cdot 2C_6H_3O_7N_3$: C, 37.04; H, 3.01; N, 21.62%).

γ-Imidazolyl-propylamin lässt sich auch durch Hydrolyse von γ-Imidazolyl-propyl-guanidin (V) darstellen.

0.2 g. Dinitrat von V und 2 g. kristallinisches Bariumhydroxyd werden in 5 c.c. Wasser gelöst, nach 2 stündigen Kochen mit Wasser verdünnt, genügend Kohlensäure eingeleitet, Bariumcarbonat abfiltriert, das Filtrat durch Schwefelsäure angesäuert, eine Lösung von Phosphorwolframsäure hinzugefügt, wobei sich ein weisser Niederschlag bildet. Dieser Niederschlag wird abfiltriert, durch Bariumhydroxyd zersetzt, von Barium völlig befreit und eine Lösung von 0.5 g. Pikrinsäure in 20 c.c. heissem Wasser hinzugefügt, wo sich gelbe Kristalle (0.25 g.) ausscheiden. Die aus Alkohol einmal und aus Wasser zweimal umkristallisierte Kristalle schmelzen bei 243–244° (unter Aufschäumen und Bräunung) die mit dem auf vorhergehende Weise bereiteten Präparat identisch sind.

Lysin-äthylester-dichlorhydrat (VIII). Wird 3.7 g. Lysin-dichlorhydrat (0.02 Mol) in 100 c.c. 3% Chlorwasserstoff enthaltendem absolutem Alkohol suspendiert und auf dem Wasserbad gekocht, so lösen sich seine Kristalle langsam auf. Nach 3 stündigem Kochen wird 20 c.c. Benzol hinzugefügt, zunächst unter normalem Druck etwa 60 c.c. destilliert und dann unter vermindertem Druck unterhalb 45° Alkohol fast vollständig abdestilliert. Wird zurückbleibende sirupöse Ester wieder in 15 c.c. Alkohol gelöst und im Eisschrank stehen gelassen, so scheiden sich weisse Kristalle aus (3.1 g.). Zur Reinigung werden sie in absoluten Alkohol gelöst und durch Zusatz von Äther ausgeschieden. Schmp. 143.5–144.5° (Aufschäumen). Sie sind hygroskopisch.

$[\alpha]_D^{17°} = +11.69$ (0.0496 g. Sbst. in 2 c.c. Alkohol). (Gef.: N, 11.49, 11.06. Ber. für $C_8H_{18}N_2O_2 \cdot 2HCl$: N, 11.34%.)

δ-(2-Mercapto-imidazolyl)-butylamin (IX). 3.7 g. Lysin-äthylester-dichlorhydrat wird in 15 c.c. Alkohol und 25 c.c. eiskaltem Wasser gelöst, durch Kältemischung auf −10 bis −15° abgekühlt und durch 120 g. 2.3% Natriumamalgam und 23 c.c. Salzsäure auf dieselbe Weise wie bei Arginin-äthylester reduziert.

Die Reaktionsflüssigkeit wird unterhalb 50° unter vermindertem Druck konzentriert. bis Kochsalz sich auszuscheiden beginnt, nach Zusatz von 4.7 g. Ammoniumrhodanid etwas erwärmt, über Nacht stehen gelassen und dann auf dem Wasserbad zur Trockne verdampft. Wird das so erhaltene Reaktionsprodukt mit 100 c.c. absolutem Alkohol erwärmt, nach dem Erkalten unlösliche anorganische Substanz abfiltriert und aus dem Filtrat Alkohol abdestilliert, so bleibt eine sirupöse Substanz zurück. Wird sie in ein wenig Wasser gelöst, nach Entfärben mit Kohle wieder konzentriert und dann 50% Kaliumcarbonat Lösung im Überschuss hinzugefügt, so scheidet sich ein weisser kristallinischer Niederschlag aus. Dieser wird abfiltriert, mit ein wenig Wasser gewaschen und getrocknet. Ausbeute 0.9 g., 26% der Theorie.

Aus Wasser wiederholt umkristallisiert, werden farblose Kristalle in Nadeln gewonnen. Schmp. 220.5–221.5° (Rötung). Wird bei der Reduktion Essigsäure statt Salzsäure benutzt, so erhält man doch ungefähr dasselbe Resultat. (Gef.: C, 48.67; H, 7.87; S, 18.05, 18.21; N, 23.85. Ber. für $C_7H_{13}N_3S$: C, 49.07; H, 7.65; S, 18.73; N, 24.55%.) 0.0849 g. Subst. wird in ein wenig Wasser gelöst und mit 0.0605 N Salzsäure titriert. Zur Neutralisierung benötigt man 8.1 c.c.; Ber. für $C_7H_{13}N_3S$ (einwertig): 8.2 c.c.

Hydrochlorid. Aus Wasser-haltigem Butylalkahol umkristallisiert, Schmp. 212–214° (Rötung und Aufschäumen).

Pikrat. Schmp. 154–155° (Aufschäumen).

δ-Imidazolyl-butylamin (X). 0.85 g. δ-(2-Mercapto-imidazoyl)-butylamin (IX) wird in 20 c.c. Wasser und 2.5 c.c. 2 N Salzäure gelöst, dazu eine Lösung von 6.8 g. Eisenchlorid in 30 c.c. Wasser hinzugefügt, auf dem Wasserbad 40 Minuten erhitzt und dann

eine 50% wässerige Lösung von 25 g. Phosphorwolframsäure hinzugegeben, wobei sich ein weisser pulveriger Niederschlag bildet.

Da dieser feinpulverige Niederschlag schwer zu filtrieren ist, so wird er durch Zentrifugieren getrennt, mit 5% Schwefelsäure gewaschen und wieder zentrifugiert. Er wird dann in Wasser suspendiert, unter Zusatz von 35 g. kristallinischem Bariumhydroxyd auf dem Wasserbad erhitzt, nach dem Erkalten filtriert, in das Filtrat genügend Kohlensäure eingeleitet, ausgeschiedener Niederschlag von Bariumcarbonat abfiltriert und das Filtrat auf dem Wasserbad konzentriert. Wird es wieder mit Salzsäure angesäuert und zur Trockne eingedampft, so bleibt kristallinisches Hydrochlorid zurück. Da dieses aber sehr hygroskopisch ist, so wird es in ein wenig Wasser gelöst und eine 50% Lösung von Kaliumcarbonat im Überschuss hinzugefügt, wobei eine ölige, stark nach Diamin riechende Substanz ausscheidet. Wird diese ölige Substanz mit alkoholhaltigem Äther mehrmal ausgezogen, die ätherische Lösung mit Natriumsulfat getrocknet und das Lösungsmittel vollständig herausgedrängt, so erstarrt sie beim Stehen allmählich zu einer kristallinischen Masse. 0.9 g. Rohprodukt wird unter vermindertem Druck destilliert und 0.6 g. Destillat vom Sdp. 204°/6 mm. gewonnen. Es ist anfangs ölig, wird aber beim Stehen gänzlich zu eine kristallinische Masse. Schmp. 51–53°.

Da das Umkristallisation schwierig ist, so wird das destillierte Produkt bei Zimmertemperatur unter vermindertem Druck über Kaliumhydroxyd aufbewahrt und dann analysiert (Gef.: C, 59.05; H, 8.53; N, 29.13. Ber. für $C_7H_{13}N_3$: C, 61.79; H, 9.64; N, 30.09%). Die Analysenwerte sind erheblich niedriger, als die berechneten. Das kommt aber vielleicht daher, dass ein Teil sich während des Wiegens in Karbonat verwandelte.

Bioxalat. 0.144 g. durch Destillation gereinigtes Imidazolylbutylamin und 0.31 g. Oxalsäure werden in 1 c.c. Wasser gelöst und nach geringerem Erwärmen Aceton hinzugefügt. Dabei scheiden sich weisse Nadeln aus. Das aus wasserhaltigem Aceton umkristallisierte Produkt schmilzt bei 168.5–170° unter Aufschäumen (Gef.: C, 41.46; H, 5.38, N, 13.28, 12.94. Ber. für $C_7H_{13}N_3 \cdot 2C_2H_2O_4$: C, 41.36; H, 5.37; N, 13.17%).

Dipikrat. Aus Wasser scheidet sich in gelben Nadeln aus. Schmp. 197.5–198.5° (Rötung und Aufschäumen).

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SYNTHESE VON IMIDAZOLDERIVATEN AUS α-AMINOSÄUREN. IV. EINE NEUE SYNTHESE VON HISTAMIN.

Von Shiro AKABORI und Shinji NUMANO.

Eingegangen am 4. November 1935. Ausgegeben am 28. März 1936.

Die Synthese von Histamin wurde, wie in der ersten Mitteilung beschrieben ist, zuerst von Windaus und Vogt[1] durch Überführung von Imidazolylpropionsäure in Histamin durch Curtiussche Reaktion ausgeführt. Später ging Pyman[2] von Diaminoaceton aus und stellte es über viele Stufen dar. Koessler und Hanke[3] wiederholten die Pymansche Methode und verbesserten dabei das Verfahren.

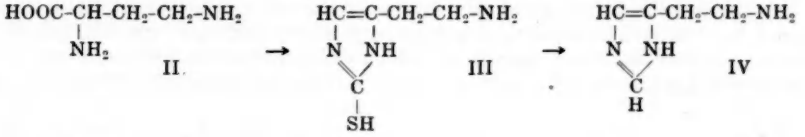
Obgleich Histamin verschiedene ausgesprochene physiologische Wirkungen auf Tiere hat und physiologisch wie pharmakologisch eine äusserst wichtige Verbindung ist[4], hat man wohl doch keine anderen Aufbauverfahren, als den oben genannten. Es gibt zwar Wege zur Darstellung des Histamins, entweder durch Entcarboxylieren von Histidin[5] oder durch Reduktion von Imidazolylacetonitril, das man durch Oxydation von Histidin mit Toluolsulfonsäure-chloramid[6] gewinnt, sie benutzten aber Histidin als Ausgangsmaterial, sodass man beide Verfahren als richtigen Aufbauverfahren nicht bezeichnen kann. Kürzlich zeigte auch Pyman[7], dass man Histamin leicht erhalten kann, wenn man Natriumrhodanid auf Diamino-ketobutan-hydrochlorid (I) einwirken lässt und das so erhaltene 2-Mercapto-histamin (III) mit Ferrichlorid oxydiert.

$$NH_2-CH_2-CH_2-CO-CH_2-NH_2\cdot 2HCl \qquad I$$

Dies kann man auch jedoch nicht als Aufbaumethode von Histamin ansehen, denn die Verbindung I wird durch Zersetzung des Histamins gewonnen. Pucher und Johnson[8] versuchten zwar aus Diäthoxy-acetessigester Histamin zu gewinnen, es gelang ihnen aber nicht. Akabori und Kaneko (III. Mitt.)[9]

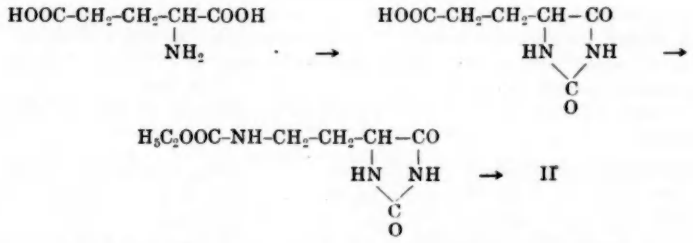
(1) *Ber.*, **40** (1907), 3691.
(2) *J. Chem. Soc.*, **99** (1911), 669.
(3) *J. Am. Chem. Soc.*, **40** (1918), 1761.
(4) S. Feldberg u. Schiff, „Histamin", Berlin (1930).
(5) Ewins u. Pyman, *J. Chem. Soc.*, **99** (1911), 339. Ackermann, *Z. physiol. Chem.*, **65** (1910), 504.
(6) Dakin, *Biochem. J.*, **10** (1916), 319; *Chem. Zentr.*, **87** (1916), II, 1142.
(7) *J. Chem. Soc.*, **1930**, 98.
(8) *J. Am. Chem. Soc.*, **44** (1922), 817.
(9) Sieh. vorangehende Mitteilung.

haben das neue Verfahren auf Arginin und Lysin angewandt und zwei höhere Homologe des Histamins erhalten. Wir haben nun auf folgende Weise aus α,γ-Diaminobuttersäure (II) Histamin dargestellt.



α,γ-Diaminobuttersäure (II) wurde zuerst von E. Fischer[10] gewonnen. Karrer und Widmer[11] gewannen *d*-α,γ-Diaminobuttersäure durch Anwendung Hoffmannschen Abbaus auf *d*-Glutamin, die Ausbeute war aber sehr schlecht.

Wir haben anfangs nach der Methode von E. Fischer *dl*-α,γ-Diaminobuttersäure synthetisch dargestellt. Da dieser Vorgang aber zu stufenartig war und die Versuche viele Schwierigkeiten machten, so sind wir von Glutaminsäure ausgegangen, indem wir dieselbe auf Dakinsche Weise[12] Hydantoinpropionsäure verwandelten und durch Anwendung Curtiusschen Abbau auf diese Säure *dl*-α,γ-Diaminobuttersäure darstellten.



Diese Methode hat auch eine nicht so gute Ausbeute, aber da man Glutaminsäure leicht erhalten kann, so ist sie als einer Laboratoriumsmethode sehr bequem. Die so erhaltene Diaminobuttersäure wurde in Äthylester verwandelt und nach der in III. Mitt. erwähnten Methode 2-Mercapto-histamin synthetisch gewonnen. Obgleich die Ausbeute hierbei sehr schlecht ist, haben wir doch Hoffnung auf bessere Ausbeute, wenn die experimentellen Bedingungen verbessert werden. 2-Mercaptohistamin kann man nach Pyman[13] mit Eisenchlorid quantitativ in Histamin (IV) verwandelt werden.

(10) *Ber.*, **34** (1901), 2900.
(11) *Helv. Chim. Acta*, **9** (1926), 301.
(12) *Am. Chem. J.*, **44** (1910), 58.
(13) *J. Chem. Soc.*, **1930**, 100.

Beschreibung der Versuche.

Hydantoinpropionsäure-äthylester. Werden 17.2 g. *dl*-Hydantoinpropionsäure (Schmp. 167–168.5°) in 60 c.c. absolutem Alkohol suspendiert, 10 g. trockener Chlorwasserstoff absorbiert und dann auf dem Wasserbad erhitzt, so löst sich die Säure allmählich auf. Nachdem sie sich gänzlich gelöst hat, wird sie weiter kurze Zeit gekocht, nach Zusatz von 40 c.c. Benzol destilliert, bis zum Sirup konzentriert und dann über Schwefelsäure unter vermindertem Druck getrocknet. Wird der Rückstand in heissem Benzol aufgenommen, der grösste Teil von Benzol abdestilliert und stehen gelassen, so scheiden sich Kristalle aus. Ausbeute 19.5 g. Aus Benzol umkristallisiert, so erfolgt Ausscheidung weisser Kristallen in Täfelchen. Schmp. 78–82°. (Gef.: N, 14.30. Ber. für $C_8H_{12}O_4N_2$: N, 14.00%.)

Hydantoinpropionsäure-hydrazid. Werden 5 g. obigen Esters und 1.4 g. Hydrazinhydrat in 5 c.c. absolutem Alkohol gelöst und gekocht, so beginnen sich nach kurzer Zeit Kristalle auszuscheiden. Nach 10 stündigem Kochen giesst man das ganze in eine Schale über, bewahrt es im Vakuumexsikkator auf und entfernt Alkohol und das überschüssige Hydrazinhydrat. Kristallisiert man einmal aus Wasser um, so erfolgen 3.3 g. Hydrazid vom Schmp. 164–167°. Ausbeute 71% der Theorie. Wird noch einmal aus Wasser umkristallisiert, so bekommt man das Produkt vom Schmp. 169–171°. (Gef.: N, 29.50. Ber. für $C_6H_{10}O_3N_4$: N, 30.11%.)

Hydantoinpropionsäure-azid. 3.7 g. obigen Hydrazids werden in 20 c.c. 2 N Salzsäure gelöst, durch Kältemischung gegen –10° abgekühlt und unter Rühren eine Lösung von 1.6 g. Natriumnitrit in 10 c.c. Wasser hineingetröpfelt. Während des Tröpfelns scheidet sich Azid in sandigen Kristallen aus. Nach beendeter Reaktion wäscht man mit ein wenig Wasser und trocknet unter vermindertem Druck über Schwefelsäure. Ausbeute 3.5 g., 89% der Theorie. Diese Substanz zersetzt sich bei 69–70° und schäumt plötzlich auf, wenn man sie auf konzentrierte Schwefelsäure fallen lässt. Da die Umkristallisierung schwer ist, wird das Azid sofort analysiert. (Gef.: N, 32.44. Ber. für $C_6H_7O_3N_5$: N, 35.53%.)

Hydantoinäthyl-carbaminsäure-äthylester (V). Werden 3.5 g. obigen Azids mit 12 c.c. absolutem Alkohol auf 40–60° erhitzt, so entwickelt sich das Gas lebhaft. Wird nach Aufhören der Gasentwicklung 1/2 Stunde gekocht, Alkohol destilliert und unter vermindertem Druck über Schwefelsäure getrocknet, so gewinnt man 3.4 g. Kristallmasse. Schmp. 82–88°. Sie ist in Wasser und Alkohol leicht löslich und in Benzol unlöslich. Da sie mit einer zähen Substanz vermischt und schwer umkristallisierbar ist, so führten wir sogleich folgenden Versuch aus.

α,γ-Diaminobuttersäure-dichlorhydrat. Wird obiges unreines Urethan sogleich mit 110 c.c. Wasser und 58 g. kristallinischen Bariumhydroxyd 8 Stunden lang gekocht, dann durch Zusatz von Wasser auf 600 c.c. verdünnt, Kohlensäure eingeleitet, Bariumcarbonat abfiltriert, das Filtrat durch Abdampfen konzentriert, unter Zusatz von wenig Schwefelsäure Barium vollständig entfernt und dann auf dem Wasserbad zur Trockne eingedampft, so bleibt zähe harzige Diaminobuttersäure zurück. Wird dieselbe in 5 c.c. konzentrierter Salzsäure gelöst und wieder konzentriert, so scheiden sich Kristalle von Diaminobuttersäure-dichlorhydrat aus. Nach Zusatz von 30 c.c. absolutem Alkohol werden die Kristalle abfiltriert. Ausbeute 1.15 g. Zersetzungspunkt 202–204°. Das aus Essigsäure, die ein wenig Salzsäure enthält, umkristallisierte Produkt hat den Zersetzungspunkt 206.3°, der mit dem des nach der Fischerschen Methode synthetisch dargestellten Produkts übereinstimmt. (Gef.: N, 14 86. Ber. für $C_4H_{10}O_2N_2 \cdot 2HCl$: N, 14.67%.)

α,γ-Diaminobuttersäure-äthylester-dichlorhydrat. Werden 5.7 g. α,γ-Diaminobuttersäure-dichlorhydrat mit 285 c.c. absolutem Alkohol, der etwa 7% Salzsäure enthält, auf dem Wasserbad gekocht, so lösen die Kristalle langsam auf. Werden diese 8 Stunden lang gekocht, unter Zusatz von 100 c.c. Benzol destilliert und schliesslich unter vermindertem Druck zum Sirup konzentriert, so erstarrt das Produkt zu einer kristallinischen Masse. Wird es aus einer Mischung von absolutem Alkohol und Benzol umkristallisiert, so erfolgen 4.7 g. Kristalle von Schmp. 173–175° (unter Aufschäumen), die in Wasser und Alkohol leicht löslich und hygroskopisch sind. (Gef. : N, 12.62. Ber. für $C_6H_{14}O_2N_2 \cdot 2HCl$: N, 12.79%.)

2-Mercapto-histamin (III). 4.6 g. obigen α,γ-Diaminobuttersäure-äthylester-dichlorhydrats werden in einer Mischung von 10 c.c. Alkohol, 30 c.c. Wasser und 10 c.c. 5 N Salzsäure gelöst, durch Kältemischung gegen –10° abgekühlt, durch 100 g. 2.3% Natriumamalgam und zur dessen Neutralisierung erforderliche Menge von 5 N Salzsäure in üblicher Weise reduziert. Nach der beendeten Reaktion wird wiederum 4 c.c. 5 N Salzsäure zugesetzt, längere Zeit stehen lassen, von Quecksilber getrennt, das Filtrat unter vermindertem Druck auf etwa 40 c.c. konzentriert, eine Lösung von 5.5 g. Ammoniumrhodanid in ein wenig Wasser zugesetzt und auf dem Wasserbad bis zu fast vollständigen Trocknen verdampft. Werden zu diesen Rückstand 70 c.c. 95% Alkohol zugesetzt, wird dann etwas erwärmt, unlösliche Substanz abfiltriert, aus dem Filtrat Alkohol abdestilliert, der Rückstand in ein wenig Wasser gelöst und 400 c.c. der bei 40° gesättigten wässerigen Quecksilber-chlorid Lösung zugesetzt, so scheidet sich ein weisser harziger Niederschlag aus. Dieser Niederschlag verwandelt sich beim Stehen allmählich in eine kristallinische Masse. Sie wird in 100 c.c. 1 N Salzsäure gelöst, durch Einleitung von Schwefelwasserstoff zersetzt und nach Abfiltrieren von Quecksilbersulfid auf dem Wasserbad zur Trockne eingedampft. Wird der Rückstand in möglichst wenig Wasser gelöst und durch Zusatz von Alkohol ausscheiden lassen, so erfolgen 0.6 g. Kristalle, die bis auf einen geringen Teil bei 245–249° schmelzen. Da die Kristalle noch ein wenig anorganische Substanz zu enthalten scheinen, so werden sie wieder in Wasser gelöst, mit Quecksilberchlorid wiederum gefallen, mit Schwefelwasserstoff zersetzt und nach Abfiltrieren von Quecksilbersulfid das Filtrat zur Trockne eingedampft. Dann wird der Rückstand aus 80%. Essigsäure umkristallisiert. Schmp. 245.5–247°. Die Analysenwerte stimmen gut mit den des Mercapto-histamin-chlorhydrat überein. Ausbeute an reinem Produkt 0.25 g. (Gef. : C, 33.76; H, 5.40; S, 17.30. Ber. für $C_5H_9N_3S \cdot HCl$: C, 33.40; H, 5.61; S, 17.85%.)

Mercapto-histamin-pikrat. Schmp. 220–222°. Nach Pyman 225° (korr.).

Histamin (IV). Werden 0.107 g. 2-Mercapto-histamin-chlorhydrat in 2 c.c. Wasser gelöst, dazu eine Lösung von 1 g. Eisenchlorid ($FeCl_3 \cdot 6H_2O$) in 15 c.c. Wasser hinzugesetzt, auf dem Wasserbad 1 Stunde erhitzt und eine Lösung von 0.3 g. Pikrinsäure in 10 c.c. heissen Wasser dazugetan, so scheiden sich gelbe Kristalle aus. Ausbeute 0.33 g., 97% der Theorie. Schmp. 231–234°. Aus Wasser einmal umkristallisiert, erhält man 0.3 g. vom Schmp. 233–235° (unter Zersetzung).

Beim Mischen mit dem aus Imidazoyl-propionsäure dargestellten Histamin-dipikrat, (von Schmp. 235–237°) zeigt sich ein Schmp. von 233–235°. (Gef. : C, 36.23; H, 2.28; N, 21.71. Ber. für $C_5H_9N_3 \cdot 2C_6H_3O_7N_3$: C, 35.84; H, 2.66; N, 22.15%.)

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ÜBER DIE SYNTHESE VON ALKOXY- UND OXY-CARBAZOLE.

Von Toshio HOSHINO und Kiyoshi TAKIURA.

Eingegangen am 4. November 1935. Ausgegeben am 28. März 1936.

3-Oxy-carbazol wird in gewöhnlicher Weise[1] aus 3-Amino-carbazol erhalten, aber nur in sehr schlechter Ausbeute, während die bekannte Darstellungsmethode von 2-Oxy-carbazol[2] sehr kompliziert ist. Daher versuchten wir die Darstellung der genannten Substanzen nach dem Verfahren von W. Borsche[3] durchzuführen.

Borsche stellte Carbazol aus Tetrahydrocarbazol, das aus Cyclohexanon-phenylhydrazon durch Erwärmen mit verdünnter Schwefelsäure erhalten wurde, durch Dehydrierung mit Bleioxyd in der Hitze dar. Diese Dehydrierungsmethode fanden wir aber besonders beim Alkoxyderivat nicht sehr geeignet. Daher versuchten wir die Dehydrierung nach dem Verfahren von Akabori und Saito[4] und zwar mittels Pd-Schwarz zusammen mit ungesättigter Verbindung als Wasserstoff-akzeptor, und erhielten gute Resultate. So stellten wir das 3- bzw. 2-Äthoxy-carbazol aus 6- bzw. 7-Äthoxy-1,2,3,4-tetrahydrocarbazol dar.

Aus 3- bzw. 2-Äthoxy-carbazol erhielten wir das 3- bzw. 2-Oxycarbazol nach dem Verfahren von Klemenc[5] und zwar durch Erhitzen mit Anilinchlorhydrat in guter Ausbeute.

Wenn man rein aber nicht so viel oben genannten Verbindungen haben will, so empfehlen wir diese Darstellungsmethode.

Der Japanischen Gesellschaft zur Förderung der Naturwissenschaften (Nippon-Gakujutu-Sinko-Kwai) danken wir ergebenst für die finanzielle Unterstützung bei dieser Arbeit.

Beschreibung der Versuche.

Die Syn hese von Carbazol. *Cyclohexanon-phenylhydrazon.* Eine Mischung äquivalenter Mengen Cyclohexanon mit Phenylhydrazin erstarrt nach anfänglicher Selbsterwärmung sehr bald zu einem schneeweissen Krystallkuchen von Phenylhydrazon. Aus

(1) Ruff u. v. Stein, *Ber.*, **34** (1901), 1683.
(2) Kehrmann u. Zweifel, *Helv. Chim. Acta*, **11** (1923), 1213; D.R.P. 522960.
(3) Borsche, *Ann.*, **359** (1908), 52.
(4) Akabori u. Saito, *Proc. Imp. Acad. Tokyo*, **6** (1930), 236.
(5) Klemenc, *Ber.*, **49** (1916), 1371.

50-proz. Alkohol umkrystallisiert. Schmp. 81–82° (Angabe von Baeyer[6] 74–75°). Die Ausbeute 95-Proz. der Theorie.

Tetrahydrocarbazol. 1.7 g. Phenylhydrazon wurden mit 20 c.c. 10-proz. Schwefelsäure vermischt, wobei unter Selbsterwärmung alles in Lösung ging. Beim Stehenlassen schieden sich allmählich farblose Tafeln aus, die aus 50-proz. Alkohol umkrystallisiert wurden. Ausbeute 1.6 g. (93-Proz. der Theorie). Schmp. 116–117° (Borsche 116°; Perkin und Plant[7] 119°).

Borsche erhitzte bei dieser Reaktion; Perkin und Plant verwandten Essigsäure statt Schwefelsäure und erhitzten auch.

Dehydrierung von Tetrahydrocarbazol (Carbazol). 0.3 g. Tetrahydrocarbazol wurden mit 0.7 g. Zimtsäure und 0.05 g. Pd-Schwarz (nach Tausz u. v. Putnosky[8]) gut vermischt in einem Reagenzrohr auf 150–200° einige Minuten lang erhitzt, wobei die anfangs grünliche Schmelze rot und klar wurde. Das Reaktionsgemisch wurde mit Alkohol gekocht und heiss filtriert. Aus dem Filtrat schieden sich farblose Blättchen aus, die abfiltriert und mit verdünnten Alkohol, Alkali und schliesslich Wasser nachgewaschen wurden. Das Produkt schmolz bei 240°. Ausbeute 0.25 g. (89-Proz. der Thorie).

Akabori und Saito benutzten als Wasserstoffakzeptor Safrol statt Zimtsäure bei dieser Reaktion, aber wir fanden die letztere Substanz viel geeigneter als die erste.

Die Synthese von 3-Äthoxy-carbazol. *p-Äthoxy-phenylhydrazin.*[9] 36 g. *p*-Phenetidin-chlorhydrat wurden mit 200 c.c. konzentrierter Salzsäure vermischt und dem Gemisch unter gutem Umrühren bei 0° eine Lösung von 20 g. Natriumnitrit in 100 c.c. Wasser zugetropft. Nach dem Ende der Reaktion wurde das Reaktionsgemisch bis −10° gekühlt, unter Umrühren eine gekühlte Lösung von 120 g. Zinnchlorür in 100 c.c. konzentrierter Salzsäure in kleinen Portionen zugetropft und dann 2 Stunden lang unter Kühlung stehengelassen. Das entstandene salzsaure Salz des Hydrazins wurde abfiltriert, mit gesättigter Kochsalzlösung nachgewaschen, unter Äther mit Alkali zersetzt, mit Äther aufgenommen und schliesslich mit festem Kali getrocknet. Beim Einengen des Äthers schied sich die Verbindung in schönen, farblosen Blättchen aus. Schmp. 74° unter Zersetzung (Angabe von Stolz auch 74°). Ausbeute 22.4 g. (71-Proz.).

Cyclochexanon-p-äthoxy-phenylhydrazon. 17 g. *p*-Äthoxy-phenylhydrazin, in 10 c.c. Alkohol gelöst, wurden mit 12 g. Cyclohexanon vermischt, wobei unter Selbsterwärmung Reaktion eintrat und bald farblose Tafeln entstanden. Umkrystallisation aus wenig Alkohol. Schmp. 77°. Ausbeute 26.5 g. (95-Proz.). Borsche gab keinen Schmelzpunkt.

6-Äthoxy-1,2,3,4-tetrahydro-carbazol. 26.5 g. des oben erhaltenen Hydrazons wurden mit 300 c.c. 10-proz. Schwefelsäure vermischt, wobei unter Selbsterwärmung alles bald in Lösung ging, aus der sich beim Abkühlen schöne farblose Nadeln ausschieden. Das Produkt schmolz bei 105–106° nach zweimaligem Umkrystallisieren aus 80-proz. Alkohol. Kocht man nach Borsche bei dieser Reaktion, so entsteht viel dunkelbraune harzige Substanz. Der Schmp. nach Borsche 87–88°.

Dehydrierung von 6-Äthoxy-tetrahydrocarbazol (3-Äthoxy-carbazol). 6-Äthoxy-1,2,3,4-tetrahydrocarbazol wurde mit 1/10 Teil Pd-Schwarz und 2 Teil Zimtsäure vermischt und unter CO_2-Atmosphäre 5–6 Minuten lang auf 200–250° erhitzt, wobei sich das Pd-Schwarz zusammen ballte und die Schmelze rot und klar wurde. Die Schmelze wurde dann vom

(6) Baeyer, *Ann.*, **278** (1894), 105.
(7) Perkin u. Plant, *J. Chem. Soc.*, **1921**, 1831.
(8) Tausz u. v. Putnosky, *Ber.*, **52** (1919), 1573.
(9) Stolz, *Ber.*, **25** (1892), 1663.

Pd-Schwarz dekantiert und erstarrte bald. Das fest gewordene Reaktionsgemisch wurde pulverisiert, mit verdünntem Alkali gut vermischt, abgesaugt und mit warmem Wasser mehrmals nachgewaschen. Dann wurde Exsiccator getrocknet, mit Petroläther gewaschen und aus 50-proz. Alkohol 2-mal umkrystallisiert. Farblose Blättchen vom Schmp. 106–107°. Ausbeute 80-Proz. der Theorie. (Gef.: N, 6.63. Ber. für $C_{14}H_{13}ON$ (211): N, 6.64%.)

3-Oxy-carbazol. 1 Mol 3-Äthoxy-carbazol wurde mit 3 Mol Anilinhydrochlorid vermischt und unter CO_2-Atmosphäre 1/2 Stunde lang auf 220° erhitzt. Das Reaktionsgemisch wurde dann mit verdünnter Salzsäure auf dem Wasserbade erhitzt und abfiltriert. Der Rückstand wurde in verdünntem Alkali gelöst, die Lösung filtriert und das Filtrat mit verdünnter Salzsäure sauer gemacht, wobei sich 3-Oxy-carbazol ausschied. Aus Alkohol farblose Blättchen vom Schmp. 256–257°. Ausbeute 50–70-Proz. der Theorie. (Gef.: N, 7.54. Ber. für $C_{12}H_{11}ON$ (185): N, 7.65%.)

Die Synthese von 2-Äthoxy-carbazol. *m*-Äthoxy-phenylhydrazin wurde aus *m*-Phenetidin in gleicher Weise wie *p*-Äthoxy-phenylhydrazin dargestellt. Die Ausbeute war 33-Proz. der Theorie. Das Produkt war ölig.

7-Äthoxy-1,2,3,4-tetrahydrocarbazol. 11.8 g. Cyclohexanon-*m*-äthoxy-phenylhydrazon, das aus 10.5 g. *m*-Äthoxy-phenylhydrazin und 11 g. Cyclohexanon erhalten worden war, wurde mit 100 c.c. 10-proz. Schwefelsäure vermischt, wobei sich unter Selbsterwärmung 7-Äthoxy-1,2,3,4-tetrahydrocarbazol in farblose Nadeln mit einer Ausbeute von 10 g. ausschied. Nach Umkrystallisieren aus 50-proz. Alkohol Schmp. 120°. (Gef.: N, 6.51. Ber. für $C_{14}H_{17}ON$ (215): N, 6.50%.)

Dehydrierung von 7-Äthoxy-tetrahydrocarbazol (2-Äthoxy-carbazol). 4.2 g. 7-Äthoxy-tetrahydrocarbazol wurde mit 12 g. Zimtsäure und 0.5 g. Pd-Schwarz vermischt, 5 Minuten lang schwach gekocht und dann wie beim 3-Äthoxy-carbazol behandelt. Nach dem Nachwaschen mit Petroläther wurde das rohe 2-Äthoxy-carbazol aus Eisessig 2-mal umkrystallisiert. Farblose Tafeln vom Schmp. 216–217°. Ausbeute 3.5 g. (Gef.: N, 6.76. Ber. für $C_{14}H_{13}ON$ (211): N, 6.64%.)

2-Oxy-carbazol. 2.1 g. 2-Äthoxy-carbazol wurden mit 3.8 g. Anilinhydrochlorid 1/2 Stunden lang im Ölbade auf 240–250° erhitzt, das Reaktionsgemisch mit heisser, verdünnter Salzsäure behandelt und dann abfiltriert. Der Rückstand wurde in verdünnter Natronlauge gelöst, abfiltriert und das Filtrat nach dem Ansäuern mit Salzsäure ausgeäthert. Nach dem Abdampfen des Äthers wurde der Rückstand aus Alkohol 2-mal umkrystallisiert. Farblose Blättchen vom Schmp. 273–274°. Ausbeute 1.3 g. Viel beständiger ist als 3-Oxy-carbazol. (Gef.: N, 7.53. Ber. für $C_{12}H_{11}ON$ (185): N, 7.65%.)

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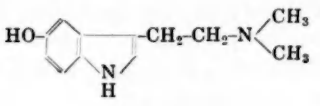
ÜBER DIE SYNTHESE DES BUFOTENIN-METHYL-ÄTHERS (5-METHOXY-*N*-DIMETHYL-TRYPTAMIN) UND BUFOTENINS.[1] (SYNTHESEN IN DER INDOL-GRUPPE. XV.)[2]

Von **Toshio HOSHINO** und **Kenya SHIMODAIRA.**

Eingegangen am 4. November 1935. Ausgegeben am 28. März 1936.

Im Zusammenhang mit Versuchen zur Synthese von Eseräthol haben wir in der vorigen Mitteilung über die Synthese des Bufotenins (5-Oxy-*N*-dimethyl-tryptamin) berichtet, die von dem Äthyl-äther ausging, der aus 5-Äthoxy-indolyl-3-äthyl-β-bromid und Dimethylamin erhalten worden war. Diesmal haben wir ganz analoger Weise den Methyl-äther von Bufotenin (5-Methoxy-*N*-dimethyl-tryptamin) hergestellt, und daraus wieder das Bufotenin erhalten.



Bufotenin

Herr Dr. R.H. Manske (Canada) hat uns jüngst (3. Oktober 1935, Ottawa) freundlicherweise darauf aufmerksam gemacht, dass wir seine beiden schönen Abhandlungen[3] übersehen hatten (Wir möchten ihm hiermit für seine Mitteilung bestens danken). In diesen Abhandlungen berichtete er über die Isolierung von *N*-Monomethyl-tryptamin (4 g.), *N*-Dimethyl-tryptamin (1 g.), Trimethyl-β-3-indolyl-äthylammonium-jodid (12.1 g.), neben regeneriertem Tryptamin (15.1 g.), aus dem Reaktionsgemisch von Tryptamin (32 g.) und Jodmethyl, ferner über die Darstellung von *N*-Dimethyl-tryptamin durch Vakuumdestillation von Trimethyl-β-3-indolyl-äthylchlorid, das aus das Jodid erhalten wird.

Im Zusammenhang mit Versuchen zur Synthese von Eserin versuchten wir die Monomethylierung von Tryptamin. Zuerst[4] liessen wir auf das Amin (1 g.) Jodmethyl reagieren und konnten dabei nur regeneriertes Amin und Trimethyl-β-3-indolyl-äthylammonium-jodid isolieren. Dann probierten wir das Verfahren von Decker und Becker und isolierten dabei 3-Phenyl-3,4,5,6-tetrahydro-4-carbolin und 3-Phenyl-4-methyl-3,4,5,6-tetrahydro-4-carbolin-jodmethylat (Herr Dr. Manske schreibt in seiner Abhandlung, dass er in diesem Falle als Hauptprodukt "a neutral cherry-red resin" erhalten hat).

(1) Wieland, Konz u. Mittasch, *Ann.*, **513** (1934), 1.
(2) Hoshino u. Shimodaira, *Ann.*, **520** (1935), 19; *Proc. Imp. Acad. Japan*, **11** (1935), 227.
(3) Manske, *Can. J. Research*, **1931**, 275, 592.
(4) Hoshino u. Kotake, *Ann.*, **516** (1935), 76.

Schliesslich[5] ist es uns gelungen nach dem Verfahren von Hinsberg die Monomethylierung von Tryptamin, sowie 5-Äthoxy-tryptamin durchzuführen und dadurch das *dl*-Eseräthol zu synthetisieren. Gleichzeitig[2] haben wir aus Indolyl-3-äthyl-β-bromid sowie 5-Äthoxy-indolyl-3-äthyl-β-bromid und Methylamin bzw. Dimethylamin das *N*-Methyl- bzw. *N*-Dimethyl-tryptamin sowie 5-Äthoxy-*N*-methyl bzw. 5-Äthoxy-*N*-dimethyl-tryptamin (Bufotenin-äthyläther) dargestellt, wie bereits oben erwähnt wurde.

N-Methyl-tryptamin: Manske Schmp. 90°, Pikrat Schmp. 191°; Hoshino und Kobayashi Schmp. 89–90°, Pikrat 190–191°. *N*-Dimethyl-tryptamin: Manske Schmp. 47°, Pikrat Schmp. 168°; Hoshino und Shimodaira Schmp. 49–50°, Pikrat (Mono-) Schmp. 170–171°. Trimethyl-β-3-indolyl-äthylammonium-jodid: Manske Schmp. 197°; Hoshino und Kotake 216–117°.

Das Trimethyl-β-3-indolyl-äthylammonium-jodid bzw. 5-Methoxy-trimethyl-β-3-indolyl-äthylammonium-jodid haben wir einfach durch Kochen der alkoholischer Lösung von Tryptamin bzw. 5-Methoxy-tryptamin mit einem Überschusse von Jodmethyl bei Anwesenheit von überschüssigem Natriumcarbonat in sehr guter Ausbeute (über 90-Proz.) erhalten, während Wieland, Konz und Mittasch[1] zur Vorsicht Talliumäthylat statt Natriumcarbonat anwandten.

Aus dem 5-Methoxy-trimethyl-β-3-indolyl-äthylammonium-jodid haben wir nach dem Verfahren von Manske das 5-Methoxy-*N*-dimethyl-tryptamin (Bufotenin-methyläther) dargestellt.

Der Stiftung des verstorbenen Herrn Tejima zur Förderung der technischen Ausbildung sind wir für die Unterstützung bei dieser Arbeit zu grossem Dank verpflichtet. Auch möchten wir Herrn Prof. R. Majima für seine Anregungen unseren besten Dank aussprechen.

Beschreibung der Versuche.

Die Synthese des 5-Methoxy-tryptophols.[2] *5-Methoxy-indolyl-(3)-essigsäure.* 30 g. 5-Methoxy-indolyl-3-acetonitril[1] (siedet bei 221°/4 mm.) werden mit Kaliumhydroxyd in Methanol-Wasser-Lösung so lange gekocht, bis kein Ammoniak mehr entwickelt wird, d.h. etwa 20 Stunden lang. Nach dem Abdestillieren des Methanols nimmt man das unveränderte Nitril mit Äther auf und macht die wässrige Schicht mit Salzsäure sauer, wobei sich anfangs eine ölige Substanz ausscheidet, die beim Stehen bald krystallinisch wird (Blättchen). Die Menge betrug ca. 23 g., der Schmp. lag bei 146–147° (Gef.: N, 7.03. Ber. für $C_{11}H_{11}O_3N$ (205): N, 6.83%).

Äthylester. Eine Lösung von 24 g. der Säure in 80 g. absolutem Alkohol wird mit HCl fast gesättigt und 1/2 Stunde lang gekocht. Der Alkohol wird in Vakuum abdestilliert und das zurückbleibende Öl mit Äther aufgenommen. Nach dem Trocknen mit Natriumsulfat wird der Äther abdestilliert und das zurückbleibende Öl in Vakuum destilliert. Die bei 202–203°/4 mm. (23 g.) übergehende Fraktion krystallisiert aus Äther

(5) Hoshino u. Kobayashi, *Ann.*, **520** (1935), 11; *Proc. Imp. Acad. Japan*, **11** (1935), 227.

in schönen farblosen Tafeln vom Schmp. 97–98° (Gef.: N, 6.32. Ber. für $C_{13}H_{15}O_3N$ (233): N, 6.03%).

Reduktion. 23 g. des Esters werden in 350 c.c. absolutem Alkohol auf dem Ölbade auf 120° erhitzt und mit 21 g. Natrium in kleinen Stückchen versetzt. Dann wird die Temperatur allmählich auf 150° gesteigert. Nach dem Verschwinden des Natriums wird etwas Wasser zugegeben, der Alkohol in Vakuum abdestilliert und nach dem Zusatz von Wasser ausgeäthert. Aus der alkalischen Lösung werden beim Ansäuern mit Salzsäure 5-Methoxy-indolyl-3-essigsäure zurückerhalten in unserem Falle 9 g. Die mit Natriumsulfat getrocknete ätherische Lösung hinterliess nach dem Abdestillieren des Lösungsmittels ein schwach braun gefärbtes Öl, das bei 194°/4 mm. schwach gelb gefärbt überging. Ausbeute 5.5 g. Pikrat: aus Benzol wurden schöne, rot gefärbte Nadeln vom Schmp. 117–118° erhalten (Gef.: N, 13.22. Ber. für $C_{11}H_{13}O_2N \cdot C_6H_3O_7N_3$ (420): N, 13.34%).

5-Methoxy-indolyl-3-äthyl-β-bromid. 2 g. 5-Methoxy-tryptophol werden in 100 c.c. absolutem Äther bei Zimmertemperatur mit 1 g. Phosphor-tribromid, gelöst in absolutem Äther, allmählich vermischt und über Nacht stehengelassen. Die Lösung wurde von der harzigen Ausscheidung abgegossen, mit Wasser und Bicarbonatlösung gewaschen und mit Kaliumcarbonate getrocknet. Nach dem Abdunsten des Äthers hinterbleibt ein fast farbloses Öl, das schon bei kurzem Erhitzen auf dem Wasserbade schwarz wird. Ausbeute 1.3 g.

5-Methoxy-*N*-dimethyl-tryptamin (Bufotenin-methyläther). 1.0 g. rohes Bromid, gelöst in 4 c.c. Methanol, wird mit 4 c.c. einer 33-proz. Dimethylamin-Lösung im Einschlussrohr im siedenden Wasserbade 15 Stunden lang erhitzt. Das Reaktionsgemisch wird mit viel verdünnter Salzsäure vermischt und durch Ausschütteln mit Äther gewaschen. Die salzsaure Schicht wird mit Kaliumcarbonat getrocknet. Nach dem Abdampfen des Äthers wird der Rückstand in Vakuum destilliert. Sdp. 208–210° (Bad) bei 4 mm. Ausbeute 0.5 g. Die Substanz krystallisiert aus Äther-Petroläther. Schöne farblose Prismen vom Schmp. 66–67° (Gef.: N, 12.71. Ber. für $C_{13}H_{18}ON_2$ (218): N, 12.85%).

Monopikrat. Aus Benzol-Aceton schöne gelb gefärbte Tafeln vom Schmp. 176–177° (Gef.: N, 15.69. Ber. für $C_{13}H_{18}ON_2 \cdot C_6H_3O_7N_3$ (447): N, 15.66%).

Krystallisiert man das Pikrat aus Methanol um, so nimmt es 1 Mol Methanol auf (Gef.: N, 14.60. Ber.: N, 14.61%).

Das Dipikrat konnten wir in diesem Falle nicht isolieren.

Jodmethylat. Aus dem Gemisch von absolutem Alkohol und Äther schöne farblose Prismen vom Schmp. 183°. Das aus natürlichen Bufotenin erhaltene *O*-Methyl-bufoteninjodmethylat schmilzt nach der Angabe von Wieland[1] und seinen Mitarbeitern bei 183–184° und das aus 5-Methoxy-tryptamin synthetisierte bei 182–183°. (Gef.: N, 7.76. Ber. für $C_{14}H_{21}ON_2J$ (360): N, 7.78%.)

Monopikrat. Aus Methylalkohol-Wasser schöne gelb gefärbte Prismen vom Schmp. 170–171° (Gef.: N, 14.98. Ber. für $C_{14}H_{21}ON_2 \cdot C_6H_2O_7N_3$ (461): N, 15.19%).

Dipikrat. Krystallisiert man das gelbe Monopikrat aus Methylalkohol-Wasser mit einem Überschuss von Pikrinsäure um, so erhält man rote Nadeln vom Schmp. 103–104°. Beim Umkrystallisieren des Dipikrats aus Benzol erhält man das gelbe Monopikrat. (Gef.: N, 16.04. Ber. fur $C_{14}H_{21}ON_2 \cdot C_6H_2O_7N_3 \cdot C_6H_3O_7N_3$ (692): N, 16.24%.)

Das Pikrat des Jodmethylates schmilzt nach der Angabe von Wieland und Mitarbeitern[1] bei 84°. Es war vielleicht ein Dipikrat.

Flavianat. Aus Methylalkohol-Wasser schöne rot gefärbte Nadeln vom Zersetzungsp. 242° (Wielands Angabe 233°).

Bufotenin. 0.45 g. Bufotenin-methyläther werden in 10 c.c. Benzol gelöst und mit 1.1 g. Aluminiumchlorid auf dem Wasserbade 15 Stunden lang gekocht wobei sich eine braunrote harzige Substanz am Boden des Kolbens ansetzt. Zum Reaktionsgemisch setzt man verdünnte Salzsäure zu, wodurch die harzige Substanz in Lösung geht, und schüttelt dann mit Äther aus. Aus der Benzol-Äther-Lösung wurde keine Substanz erhalten.

Nach Zugabe von Natronlauge bis zur alkalischen Reaktion wurde durch Ausäthern eine ganz kleine Menge von Ausgangsmaterial zurückerhalten. Die alkalische Lösung wurde nochmals mit Salzsäure sauer und mit Natriumbicarbonat wieder schwach alkalisch gemacht, wobei sich die Lösung trübte. Nach dem erschöpfenden Extrahieren mit peroxydfreiem Äther wurde der schwach gelb gefärbte Äther mit Natriumsulfat getrocknet. Nach dem Abdampfen hinterblieben 0.35 g. einer öligen Substanz.

Dipikrat. Aus Methylalkohol schöne, rot gefärbte Prismen vom Schmp. 177–178°.

Monopikrat. Beim Kochen in Benzol geht das rot gefärbte Dipikrat in ein gelbes über und schmilzt auch bei 177–178°.

Die beiden Pikrate sind jeweils ganz identisch mit den betreffenden Pikraten von Bufotenin, das früher[2] aus dem Bufotenin-äthyläther erhalten worden war.

5-Methoxy-trimethyl-β-3-indolyl-äthylammonium-jodid. 1.5 g. 5-Methoxy-tryptamin, gelöst in 30 c.c. absolutem Alkohol, wurden mit 5 g. Jodmethyl vermischt und bei Anwesenheit von 4.5 g. wasserfreiem Natriumcarbonat 5 Stunden lang auf dem Wasserbade gekocht. Das Reaktionsgemisch wurde heiss abgesaugt, der Rückstand nochmals mit absolutem Alkohol gekocht und heiss abgesaugt. Wird das gesamte Filtrat eingeengt und stehen gelassen, so scheiden sich schöne, farblose, grosse Nadeln aus. Der Körper schmilzt bei 183° und die Mischprobe mit 5-Methoxy-bufotenin-jodmethylat bei gleichen Temperatur. Die Ausbeute betrug 1.8 g. Nach weiteren Einengen der Mutterlauge wurden noch 0.7 g. erhalten.

Trimethyl-β-3-indolyl-äthylammonium-jodid wurde ganz analogerweise aus Tryptamin, ebenfalls mit guter Ausbeute erhalten.

5-Methoxy-trimethyl-β-3-indolyl-äthylammonium-chlorid. 1.6 g. 5-methoxy-trimethyl-β-3-indolyl-äthylammonium-jodid, gelöst in 20 c.c. absolutem Alkohol, wurden mit 6 g. AgCl am Rückflusskühler 3 Stunden lang erhitzt, heiss abfiltriert, der Rückstand nochmals mit absolutem Alkohol gekocht und heiss abfiltriert. Engt man das gesamte Filtrat stark ein und lässt über Nacht stehen, so scheiden sich schöne, sehr grosse, farblose Tafeln vom Schmp. 144° aus. Die Menge betrug 0.7 g. Aus der Mutterlauge isolierten wir noch 0.5 g. der gleichen Krystalle. (Gef.: N, 10.13. Ber. für $C_{14}H_{21}ON_2Cl$ (269): N, 10.43%.)

Monopikrat schmilzt bei 170–171° und ist identisch mit dem aus 5-Methoxy-bufotenin-jodmethylat erhaltenen (Mischprobe).

5-Methoxy-*N*-dimethyl-tryptamin aus 5-Methoxy-trimethyl-β-3-indolyl-äthyl-ammonium-chlorid: 0.6 g. 5-Methoxy-trimethyl-β-3-indolyl äthylammonium-chlorid wurden im Hochvakuum auf 240–250° erhitzt, wobei unter Aufschäumen ein gelb gefärbtes Öl überging, während eine rotbraun gefärbte harzige Substanz zurückblieb. Das Öl wurde in einer kleinen Menge von Methylalkohol gelöst und Pikrinsäure zugesetzt. Das gelb gefärbte Pikrat schmolz bei 172° und seine Menge betrug 0.1 g. Nach dem Umkrystallisieren aus Methylalkohol schmolz es bei 174–175° und die Mischprobe mit dem Pikrat (174–175°) von 5-Methoxy-*N*-dimethyl-tryptamin ergab keine Erniedrigung.

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STUDIES ON QUINOXALINE COLOURS.

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Quinoxaline colours belong to azine colours, and are derivatives of quinoxaline (according to Hinsberg). The only technically important dyestuff of this series is Flavinduline (B) $C_{26}H_{17}N_2Cl$ which was discovered by C. Schraube in 1893[1], and was obtained by the action of *o*-amidodiphenylamine on phenanthraquinone in glacial acetic acid solution, followed by boiling the reaction products with dilute hydrochloric acid.

The papers related to the quinoxaline colours which have been published are very poor and a few investigators have described only unsatisfactorily Flavinduline and its properties.

The present studies have been undertaken with the view to pursue the study in greater detail and to get more exact information as to the properties of quinoxaline and its derivatives, and especially as to their dyeing character which has been explained by "chromophore theory" or "quinoid theory".

First of all, the three condensations described in the experimental parts have been studied.

Experimental.

I. The reaction of phenanthraquinone on *o*-amidodiphenylamine in glacial acetic acid solution. Preparation of the dyestuffs. *Chloride.* A mixture of 1 part of *o*-amidodiphenylamine (5 g.), 1 part of phenanthraquinone (5 g.) and about 20 parts of glacial acetic acid (100 g.) is heated on the water bath until a sample shows no increase in intensity of colour. The melt is then boiled with 20 times its volume of water, acidified with HCl (38%, 30 g.), cooled, and filtered. The dye is precipitated from the filtrate with zinc chloride.

Bromide. According to the formation process of the chloride, the melt is boiled with HBr solution (48%, 40 g. in 1500 g. water), cooled, and filtered. The dyestuff is precipitated.

Iodide. The melt is boiled with HI solution (57%, 60 g. in 1500 g. water), cooled, and filtered. The dyestuff is precipitated.

Molecular weight.

		Calculated	Found
Chloride	$C_{26}H_{17}N_2Cl \cdot {}^1/_2ZnCl_2$	460.5	448.1
Bromide	$C_{26}H_{17}N_2Br$	437.0	420.3
Iodide	$C_{26}N_{17}N_2I$	484.0	468.1

(1) E.P. 18374 (1893); U.S.P. 543784 (1975).

Analytical data (%).

	$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl_2$		$C_{26}H_{17}N_2Br$		$C_{26}H_{17}N_2I$	
	Calculated	Found	Calculated	Found	Calculated	Found
C	67.75	66.20	71.39	71.20	64.46	64.25
H	3.69	4.60	3.89	5.30	3.51	4.09
N	6.08	6.79	6.39	6.20	5.78	6.11
Cl	15.42	15.77	Br 18.3	18.13	I 26.23	26.19

Properties. *Form and colour.*

$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl$	yellowish red needles;
$C_{26}H_{17}N_2Br$	brownish red needles;
$C_{26}H_{17}N_2I$	glistening black needles.

Melting point. Melting points of these compounds are over 285°C., and difficult to be determined exactly.

Solubility.

Solvent	$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{26}H_{17}N_2Br$	$C_{26}H_{17}N_2I$
Water	very sol.	not very sol.	sparingly sol.
Alcohol	very sol.	sol.	sol.
Aniline	very sol.	very sol.	very sol.
Chloroform	sol.	sol.	sol.
Nitrobenzene	sol.	sol.	sol.
Acetone	sol.	sol.	sol.
Glacial acetic acid	very sol.	very sol.	very sol.
Benzene	insol.	insol.	insol.
Ether	insol.	insol.	insol.

Colour reaction in aqueous solutions.

Solvent	$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{26}H_{17}N_2Br$	$C_{26}H_{17}N_2I$
H_2O	reddish brown	reddish yellow	yellow
NaOH	greyish green precipitate	bluish yellow precipitate	yellowish brown precipitate
HCl	reddish yellow	yellow	pale yellow
H_2SO_4 (conc.)	bluish red	brownish red	brownish red

Dyeing.

	Cotton	Silk	Wool
$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl_2$	yellowish brown	reddish yellow	brown
$C_{26}H_{17}N_2Br$	pale yellowish brown	reddish yellow	yellowish brown
$C_{26}H_{17}N_2I$	pale yellow	reddish yellow	greenish brown

These Dyestuffs have good affinity, especially for silk and wool.

Fastness.

	$C_{26}H_{17}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{26}H_{17}N_2Br$	$C_{26}H_{17}N_2I$
Light	good	good	good
Washing	good	good	good
Soap	moderate	moderate	moderate
Alkali	moderate	moderate	moderate
Acetic acid	good	good	good
Sulphuric acid	good	good	good

II. The reaction of phenanthraquinone on o-amidomonomethylaniline in glacial acetic acid solution. Preparation of the dyestuffs. *Chloride.* A mixture of 1 part of *o*-aminomonomethylaniline (5 g.), 1 part of phenanthraquinone (5 g.), and about 20 parts of glacial acetic acid (100 g.) is heated on the water bath until a sample shows no increase in intensity of colour. The melt is then boiled with HCl solution (38%, 25 g. in 1500 c.c. water), and filtered. The dye is precipitated from the filtrate with zinc chloride.

Bromide. According to the formation process of the chloride, the melt is boiled with HBr solution (48%, 45 g. in 1500 c.c. water), and filtered while hot. The dyestuff is precipitated on cooling.

Iodide. The melt is boiled with HI solution (57%, 60 g. in 1500 c.c. water).

Molecular weight.

		Calculated	Found
Chloride	$C_{21}H_{15}N_2Cl\cdot{}^1/_2ZnCl$	397.59	406.38
Bromide	$C_{21}H_{15}N_2Br$	374.91	382.80
Iodide	$C_{21}H_{15}N_2I$	421.93	430.10

Analytical data.

	$C_{21}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$		$C_{21}H_{15}N_2Br$		$C_{21}H_{15}N_2I$	
	Calculated	Found	Calculated	Found	Calculated	Found
C	63.39	64.09	67.21	66.89	59.72	59.04
H	3.77	4.02	4.00	4.81	3.55	4.16
N	7.40	7.20	7.46	7.53	6.63	6.64
Cl	17.80	18.05	Br 21.03	20.89	I 30.08	29.38
Zn	8.22	6.88				

Properties. *Form and colour.*

$C_{21}H_{15}N_2Cl \cdot {}^1/_2ZnCl_2$	brown needles ;
$C_{21}H_{15}N_2Br$	yellow needles ;
$C_{21}H_{15}N_2I$	glistening brownish red needles.

Melting point (Decomposition point).

$C_{21}H_{15}N_2Cl \cdot {}^1/_2ZnCl_2$	200–205°C.
$C_{21}H_{15}N_2Br$	216–217°C.
$C_{21}H_{15}N_2I$	195–200°C.

Solubility.

Solvent	$C_{21}H_{15}N_2Cl \cdot {}^1/_2ZnCl_2$	$C_{21}H_{15}N_2Br$	$C_{21}H_{15}N_2I$
Water	sol.	sol.	sol.
Alcohol	sol.	sol.	sol.
Aniline	very sol.	very sol.	very sol.
Chloroform	sol.	sol.	sol.
Nitrobenzene	sol.	sol.	sol.
Acetone	sol.	sol.	sol.
Glacial acetic acid	sol.	sol.	sol.
Benzene	insol.	insol.	insol.
Ether	insol.	insol.	insol.

Colour reaction in aqueous solution.

Solvent	$C_{21}H_{15}N_2Cl \cdot {}^1/_2ZnCl_2$	$C_{21}H_{15}N_2Br$	$C_{21}H_{15}N_2I$
H_2O	yellow, with greenish fluorescence	yellow, with greenish fluorescence	yellow, with greenish fluorescence
NaOH	pale green precipitate	pale yellowish brown precipitate	pale greyish yellow precipitate
HCl	reddish yellow	reddish yellow	reddish yellow
H_2SO_4 (conc.)	brownish red	brownish red	brownish red

Dyeing.

	Cotton	Silk	Wool
$C_{21}H_{15}N_2Cl \cdot {}^1/_2ZnCl$	brown	yellow	yellow
$C_{21}H_{15}N_2Br$	brown	yellow	yellow
$C_{21}H_{15}N_2I$	brown	yellow	yellow

These dyestuffs have good affinity for cotton.

Fastness.

	$C_{21}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$			$C_{21}H_{15}N_2Br$			$C_{21}H_{15}N_2I$		
	Cotton	Silk	Wool	Cotton	Silk	Wool	Cotton	Silk	Wool
Light	good	bad	bad	good	bad	bad	good	bad	bad
Washing	moderate	bad	bad	mod.	bad	bad	mod.	bad	bad
Soap	bad	bad	bad	bad	bad	bad	bad	bad	bad
Acetic acid	good	bad	bad	good	bad	bad	good	bad	bad
Sulphuric acid	moderate	mod.	mod.	mod.	bad	bad	mod.	mod.	mod.

III. The reaction of naphthoquinone on *o*-amidodiphenylamine in glacial acetic acid solution. Preparation of the dyestuffs. *Chloride.* A mixture of 1 part of *o*-amidodiphenylamine (5 g.), 1 part of naphthoquinone (5 g.) and about 20 parts of glacial acetic acid (100 g.) is heated on the water bath until the sample shows no increase in intensity of colour. The melt is then boiled with 20 times its volume of water acidified with HCl (38%, 30 g.), cooled, and filtered. The dye is precipitated from the filtrate with zinc chloride.

Bromide. According to the formation process of the chloride, the melt is boiled with HBr solution (48%, 40 g. in 1500 g. water), filtered, and cooled. The dyestuff is precipitated.

Iodide. The melt is boiled with HI solution (57%, 60 g. in 1500 g. water).

Molecular weight.

		Calculated	Found
Chloride	$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	410.75	392.5
Bromide	$C_{22}H_{15}N_2Br$	387.06	378.8
Iodide	$C_{22}H_{15}N_2I$	434.07	430.6

Analytical data (%).

	$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$		$C_{22}H_{15}N_2Br$		$C_{22}H_{15}N_2I$	
	Calculated	Found	Calculated	Found	Calculated	Found
C	64.27	64.30	68.21	67.51	60.82	61.03
H	3.68	3.63	3.91	5.57	3.48	3.38
N	6.82	6.80	7.24	7.23	6.45	6.39
Cl	17.26	17.52	Br 20.65	19.74	I 29.24	29.16
Zn	7.95	7.58				

Properties. *Form and colour.*

$C_{21}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	madder brown needles;
$C_{22}H_{15}N_2Br$	vistoris lake needles;
$C_{22}H_{15}N_2I$	vandyke red needles.

Melting point (decomposition point).

$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	278—279°C.
$C_{22}H_{15}N_2Br$	281—282°C.
$C_{22}H_{15}N_2I$	220—221°C.

Solubility.

Solvent	$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{22}H_{15}N_2Br$	$C_{22}H_{15}N_2I$
Water	very sol.	very sol.	very sol.
Alcohol	sol.	sol.	sol.
Aniline	very sol.	very sol.	very sol.
Chloroform	insol.	insol.	insol.
Nitrobenzene	sol.	sol.	sol.
Acetone	sol.	sol.	sol.
Glacial acetic acid	sol.	sol.	sol.
Benzene	insol.	insol.	insol.
Ether	insol.	insol.	insol.

Colour reaction in aqueous solution.

Solvent	$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{22}H_{15}N_2Br$	$C_{22}H_{15}N_2I$
H_2O	yellowish red	brownish yellow	reddish yellow
NaOH	bluish yellow (black ppt.)	pale yellow (yellowish green ppt.)	yellow (red ppt.)
HCl	reddish yellow	reddish yellow	pale yellow
H_2SO_4	brownish red	brownish red	pale red

Dyeing.

	Cotton	Silk	Wool
$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	pale sudan brown	capucin yellow	deep fresh colour
$C_{22}H_{15}N_2Br$	sudan brown	golden yellow	ocher red
$C_{22}H_{15}N_2I$	pale sudan brown	pale capucin yellow	seashell colour

These dyestuffs have good affinity for silk, wool, and especially for cotton.

Fastness.

		$C_{22}H_{15}N_2Cl\cdot{}^1/_2ZnCl_2$	$C_{22}H_{15}N_2Br$	$C_{22}H_{15}N_2I$
Light	Cotton	good	good	good
	Silk	moderate	moderate	moderate
	Wool	moderate	moderate	moderate
Washing	Cotton	good	good	good
	Silk	bad	bad	bad
	Wool	bad	bad	bad
Soap	Cotton	bad	bad	bad
	Silk	bad	bad	bad
	Wool	bad	bad	bad
Acetic acid	Cotton	good	good	good
	Silk	bad	bad	bad
	Wool	moderate	moderate	moderate
Sulphuric acid	Cotton	good	good	good
	Silk	bad	bad	bad
	Wool	moderate	moderate	moderate

STUDIES ON THE STRUCTURE OF STRYCHNINE. III. STRYCHNINOLONE AND ITS DERIVATIVES.

By **Munio KOTAKE** and **Tadahiro MITSUWA.**

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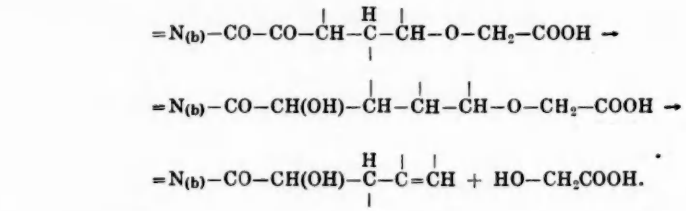
Leuchs and others discovered an important reaction : strychninolic acid is decomposed into strychninolone and glycolic acid when treated with alkali. Although strychninonic acid can hardly be broken up to produce glycolic acid by alkali, if it is reduced to strychninolic acid, the latter easily gives glycolic acid even by the action of dilute alkali. It is undoubtedly due to the fact that the carbonyl group of strychninonic acid is reduced to an alcoholic group. It must have therefore been assumed that, according to Leuchs's or Robinson's formula as shown below, the influence of the carbonyl or the alcohol group should extend so far as to the third carbon atom with the glycolic acid group.



It seemed to be rather unreasonable. Further careful studies on strychninolone, produced by the above reaction, might very likely throw light upon the matters in question. For this reason the present investigation was started.

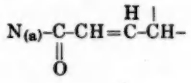
According to Leuchs's method, strychnine was oxidized with potassium permanganate in acetone solution and the formed precipitate was extracted with water. The aqueous solution was then extracted with chloroform. From the chloroform layer dihydroxystrychnine ($C_{21}H_{24}N_2O_4$, needles) was isolated as a by-product. Its hydrochloride crystallises in needles, and decomposes at 212°; its iodomethylate is also crystalline and melts at 322°. Thus it is shown that in Leuchs's oxidation the double bond is also first to be oxidized.

Leuchs informed that, besides strychninolone, the a-form (m.p. 228–231°, [α]-112–4°), which was obtained from strychninolic acid treated with alkali, there were two more isomers: when the a-form was shaken with 0.5 N alkali, the b-form (m.p. 228–230°, [α]-37°) was obtained; and when the a-form was heated with methyl alcoholic ammonia, the c-form (m.p. 252°, [α]-176°). However, there is still some doubt about the identity of the reduction products of these compounds of Leuchs's. Therefore these isomers were first of all subjected to further investigation.

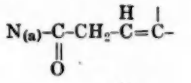
As Leuchs reported, strychninolone melting at 228–230° was obtained by the action of alkali upon strychninolic acid, but when it was subjected to fractional crystallization, it was found that the substance melting at 238–240°, which was designated strychninolone-β, was separated from the less soluble portion, and the substance melting at 224°, which was designated strychninolone-α, was separated from the more soluble portion. It is interesting that these two compounds have the same formula $C_{19}H_{18}N_2O_3$ and are reduced to a dihydro-compound by catalytic reduction.

It is considered, therefore, that the substance melting at 228–230° or Leuchs's strychninolone-a is a mixture of strychninolone-α (m.p. 224°) and strychninolone-β (m.p. 240°). Since these two substances give the same reduction product, they are believed to be isomeric with each other, simply showing the difference in the position of a double bond. This consideration well

agrees with the following fact. Leuchs already reported that when acetyl-brucinolone is oxidized with potassium permanganate, there are obtained barium salts of two isomeric carboxylic acids, each of which produces oxalic acid and malonic acid. Taking the above-mentioned fact into account, the two following formulas for the two isomeric strychninolones may be considered:

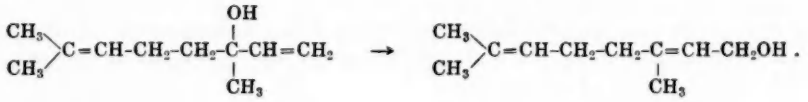


I

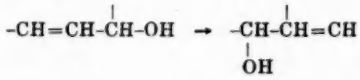


II

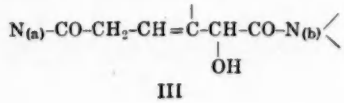
If formula II represents strychninolone-α, formula I belongs to strychninolone-β. (Such a representation is convenient to the following explanation.) The mixture of the two compounds which were found to melt at 228–230° was shaken with 0.5 N NaOH solution for five days, no visible reaction occurred. But when it was warmed with 10% KOH solution in the presence of a small amount of alcohol, γ-isomer $C_{19}H_{18}N_2O_3$ melting at 254° was obtained. It forms not only dihydro-derivative $C_{19}H_{20}N_2O_3$ but also mono-acetyl-derivative $C_{21}H_{20}N_2O_4$, and it is therefore no doubt an isomer. Since its reduction product is not identical with that of other isomers, it cannot but be considered an isomer caused by the shift of the hydroxyl group. For such an explanation the linalool-geraniol isomerism is often taken as an example:



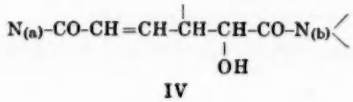
If it is assumed that such an isomeric change occurs between strychninolone-α and strychninolone-γ, the isomerism will be quite readily understood:



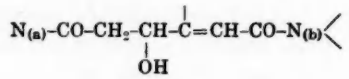
If the assumption be correct, strychninolone-α, strychninolone-β, and strychninolone-γ will be represented by formulas III, IV, and V, respectively, and the number of carbon atoms between $N_{(a)}$ and $N_{(b)}$ of the strychninolone molecule will be six:



III

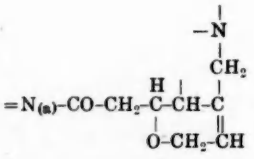


IV



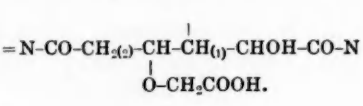
V

Consequently there must be an atomic group represented by VI in the strychnine molecule.

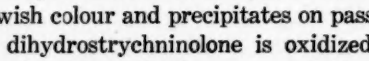


VI

By the same explanation, the fact that glycolic acid does not split from strychninonic acid but does from strychninolic acid, may be well understood. If strychninonic acid forms an enol structure in an alkaline medium, the hydrogen atom of $C_{(1)}$ migrates to the oxygen atom of the adjacent carbonyl group and there will be no opportunity for glycolic acid to be split off. Hence it is regarded that strychninolic acid does not form an enol structure, the hydrogen atom remaining in $C_{(1)}$, and it splits readily glycolic acid.

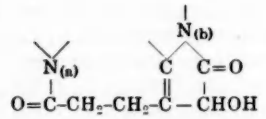


Now a question arises whether such a compound as strychninonic acid forms an enol structure or not. Strychninone $C_{19}H_{16}N_2O_3$ (m.p. 273°), obtained from strychninolone by oxidation with chromic acid, readily dissolves in alkali in slightly yellowish colour and precipitates on passing carbon dioxide in the solution. When dihydrostrychninolone is oxidized with chromic acid, dihydrostrychninone is also obtained ; the compound dissolves slowly in alkali to a colourless solution, and, moreover, does not precipitate with carbon dioxide. It may be assumed that the hydrogen atom of $C_{(2)}$ may be removed in order to split glycolic acid from strychninolic acid molecule, the keto form,

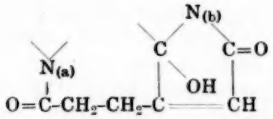


. If the assumption mentioned above is correct, glycolic acid also has to split off from strychninonic acid, but actually the reaction does not occur.

Two following isomeric formulas for strychninolones may also be considered :



VII



VIII

Really strychninolone-δ, an isomer melting at 286°, is obtained from strychninolone-a by heating it with sodium ethylate. Strychninolone-δ can not be reduced in the presence of Pd at room temperature, but gives an acetyl derivative. Considering the fact that neostrychnine and Tafel base are not easily reduced at room temperature, the position of the double bond of these compounds may be the same with that of strychninolone-δ.

Leuchs's method, action of methyl alcoholic ammonia upon strychninolone-a, was repeated and the neutral substances in the reaction product were treated with hot water. From the more soluble portion was obtained strychninolone-γ, and from the less soluble portion a new isomer, which was recrystallized from water and melted at 241–243°. The isomer, expressed by the name strychninolone-ε, was readily reduced by catalytic reduction and gave a mono-acetyl-derivative. Since strychninolone-γ is obtained by the same method, strychninolone-ε is regarded to be produced also by the shift of OH-group. Therefore strychninolone-ε is represented by formula VIII and consequently strychninolone-δ by formula VII.

Supposing the ring of the molecule opens in one position and closes in another, one more isomer can be obtained. The confirmation of this idea is left for future investigation.

Melting points of strychninolone isomers and their derivatives

Strychninolone		Dihydro-derivative	Acetyl derivative
α $C_{19}H_{18}N_2O_3$	224°	274°	240–243°
β $C_{19}H_{18}N_2O_3$	238–240°	274°	253°
γ $C_{19}H_{18}N_2O_3$	254°	215–217°	260°
δ $C_{19}H_{18}N_2O_3 \cdot 3H_2O$	286°	—	340–350°
ε $C_{19}H_{18}N_2O_3 \cdot H_2O$	240–243°	257°	214–215°

Experimental Part.

Dihydroxy-strychnine. Strychnine was oxidized with potassium permanganate in acetone solution. In order to separate[1] the oxidized substance, the precipitate was extracted with cold water and the aqueous extract was shaken with chloroform. When the solvent

(1) *Ber.*, **41** (1908), 1711; *ibid.*, **46** (1913), 3693.

was distilled off, needle crystals were obtained. This substance was recrystallized from methanol. It bubbles at 100°, solidifies again on further heating, contracts at about 155°, and melts finally at 240°. The crystals obtained from methanol solution gave the following results by analysis: Found: C, 66.15, 66.27; H, 6.84, 6.60. Calc. for $C_{21}H_{24}N_2O_4 \cdot CH_3OH$: C, 66.00; H, 7.00%. The crystals from aqueous solution showed the following results by analysis: Found: C, 61.39, 61.23; H, 7.21, 7.12. Calc. for $C_{21}H_{24}N_2O_4 \cdot 2^1/_2H_2O$: C, 61.02; H, 7.02%. The above substance was dehydrated by heating in the xylene bath under reduced pressure and subjected to analysis: 3.618 mg. gave 9.070 mg. CO_2 and 2.264 mg. H_2O. Found: C, 68.37, 68.12; H, 7.00, 6.76. Calc. for $C_{21}H_{24}N_2O_4$: C, 68.5; H, 6.50%.

Dihydroxystrychnine Hydrochloride. When dihydroxystrychnine was dissolved in hydrochloric acid and the solution evaporated, needle crystals were obtained. They were recrystallized from water. Needles, decomposing at 212° with bubbling: (Found: C, 58.93, 59.16; H, 6.64, 6.68. Calc. for $C_{21}H_{24}O_4 \cdot HCl \cdot H_2O$: C, 59.64; H, 6.39%).

Dihydroxystrychnine-iodomethylate. Dihydroxystrychnine in methanol was treated with methyliodide, and dihydroxystrychnine iodomethylate was obtained. It was recrystallized from water, m.p. 322°. (Found: C, 52.30, 52.18; H, 5.59, 5.21. Calc. for $C_{21}H_{24}N_2O_4 \cdot CH_3I$: C, 51.75; H, 5.29%.)

Purification of Strychninolones (Separation of α- and β-Isomers). Strychninolone obtained from strychninolic acid by the action of cold alkali was found to melt at 215–225°. It was subjected to fractional crystallization from methanol. The first crop of crystals melted at 238–240°, and further four crops, melting at 235–237°, 232–234°, 228–230°, and 222–224°, respectively, were obtained from the mother liquor. The first crop melting at 238–240° was recrystallized from ethyl alcohol, methanol, and other solvents, but its melting point was not raised. The portion melting at 222–224° was recrystallized from alcohol and its melting point was found to be 223–224°. The crops obtained between these two crops were finally separated into the above two substances by repeated crystallization. The substances melting at 223-224° or α-isomer was analyzed: Found: C, 70.38, 70.47; H, 6.03, 6.07. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80; H, 5.59%. The substance melting at 238-240° or β-isomer was analyzed as follows: Found: C, 70.77, 70.70; H, 5.82, 5.81. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80; H, 5.59%.

Catalytic Reduction of Strychninolone-α and Strychninolone-β. Strychninolone-α (m.p. 224°), strychninolone-β (m.p. 240°) and strychninolone-a (m.p. 228–230°) were respectively dissolved in alcohol or glacial acetic acid and shaken in the current of hydrogen gas for three hours in the presence of Pd-catalyst. When the absorption of hydrogen ceased, the reaction mixture was filtered in order to separate Pd, and the solvent was distilled, when the reduction product was obtained in crystalline form. It was recrystallized from methanol. The above-mentioned three substances gave the identical reduction product; needles melting at 274°. (Found: C, 70.77, 70.78; H, 6.15, 6.16. Calc. for $C_{19}H_{20}N_2O_3$: C, 70.37; H, 6.17%.)

Acetylation of Strychninolone-α. Strychninolone-α (0.5 g.) in 10 c.c. of acetic anhydride with a small amount of anhydrous sodium acetate was heated at 100° for four hours provided with an air condenser. After removal of acetic anhydride under reduced pressure, the reaction mixture was dissolved in water and shaken with chloroform. The chloroform layer was separated from aqueous solution and the solvent was distilled. When a few drops of alcohol was added to the residue, a crystalline substance appeared. It was recrystallized from ethyl alcohol or methanol. Needles, melting at 240–243°. (Found: C, 68.89; H, 6.05. Calc. for $C_{21}H_{20}N_2O_4$: C, 69.23; H, 5.52%.)

Acetylation of Strychninolone-β. The procedure of the acetylation of strychninolone-α was followed in every particular. Needles, m.p. 253°. (Found: C, 69.40, 69.23; H, 5.94, 5.93. Calc. for $C_{21}H_{20}N_2O_4$: C, 69.23; H, 5.52%.)

Formation of Strychninolone-γ. To strychninolone-a was mixed with 10% potassium hydroxide solution and a few drops of alcohol, and the mixture was warmed on the water bath, when the solid was dissolved in a short time. After cooling the mixture, it was treated with hydrochloric acid, when there appeared a white precipitate. Allowing the precipitate to settle down for one day, it was separated by filtration and recrystallized from alcohol. Needles, m.p. 254°; yield 70%. (Found: C, 71.15, 70.81; H, 6.05, 6.10. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80; H, 5.59%.)

Catalytic Reduction of Strychninolone-γ. Strychninolone-γ, dissolved in glacial acetic acid, was shaken in the current of hydrogen in the presence of catalytic Pd. When it ceased to absorb hydrogen, the reaction mixture was filtered to remove the catalyst and the solvent was distilled under reduced pressure, when crystalline residue was obtained. It was recrystallized from ethyl alcohol and methanol successively, prisms melting at 215°. (Found: C, 70.13, 69.90; H, 6.31, 6.46. Calc. for $C_{19}H_{20}N_2O_3$: C, 70.37; H, 6.17%.)

Acetylation of Strychninolone-γ. To strychninolone-γ, (0.4 g.), was added 10 c.c. of acetic anhydride and a small amount of anhydrous sodium acetate. The mixture was warmed at 100° for four hours, using an air condenser. Then acetic anhydride was distilled under reduced pressure, the residue dissolved in water, and the solution shaken with chloroform. When the chloroform layer was separated from the aqueous solution, the solvent distilled, and a few drops of alcohol were added to the residue, crystals separated out. They were recrystallized from ethyl alcohol or methanol. Needles, m.p. 260°. (Found: C, 69.07, 69.24; H, 6.00, 5.98. Calc. for $C_{21}H_{20}N_2O_4$: C, 69.23; H, 5.52%.)

Formation of Strychninolone-δ: Reaction of Sodium Ethylate upon Strychninolone-a. To 1 g. strychninolone-a was added a solution of sodium ethylate (prepared from 1 g. of sodium) in absolute alcohol, and the mixture was heated on the water bath under a reflux condenser for two hours. Then the alcohol was distilled. When a small amount of water, a few drops at a time, was added to the residue, needle crystals appeared. It was recrystallized from dilute alcohol. It was found to melt at 285–286° with bubbling: (Found: C, 60.54, 60.36; H, 6.46, 6.66. Calc. for $C_{19}H_{18}N_2O_3 \cdot 3H_2O$: C, 60.63; H, 6.38%). When it was dehydrated under reduced pressure on a xylene bath, 4.253 mg. of the substance lost 0.554 mg. or 13.1% of the original weight, whereas the theory requires 14%: (Found: C, 70.36, 70.68; H, 6.01, 5.92. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80, H, 5.59%).

It was subjected to reduction in the current of hydrogen gas in the presence of Pd but no reaction was observed.

Acetyl-strychninolone-δ. For the preparation of this compound the directions given in the case of acetyl-strychninolone-γ were followed. It was obtaind in needles and recrystallized from methanol; its melting point was above 340°: (Found: C, 65.54, 65.49; H, 6.07, 5.54; H_2O, 4.0. Calc. for $C_{21}H_{20}N_2O_4 \cdot H_2O$: C, 65.96; H, 5.54; H_2O, 4.8. Calc. for $C_{23}H_{22}N_2O_5 \cdot H_2O$: C, 65.10; H, 5.66; H_2O, 4.2%.)

Action of Methyl Alcoholic Ammonia upon Strychninolone-a (Formation of Strychninolone-ε). To strychninolone-a was added methyl alcoholic ammonia (saturated at 20°) and the mixture was heated in a sealed tube for three hours. The sealed tube was allowed to cool overnight and opened. When methanol was evaporated, crystals were obtained. They were treated with hydrochloric acid and shaken with chloroform; when

the chloroform layer was separated and evaporated, crystals melting at 240° separated out. They were treated with hot water and subjected to fractional crystallization. From the more soluble part, fine needles were obtained by cooling the hot solution. They were recrystallized from water and found to melt at 240–243°C: (Found: C, 67.50; H, 6.21; H_2O, 5.4. Calc. for $C_{19}H_{18}N_2O_3 \cdot H_2O$: C, 67.05; H, 5.99; H_2O, 5.3%). The dehydrated substance obtained by warming in a xylene bath under reduced pressure was found to melt at 208°. (Found: C, 70.51, 70.37; H, 6.09, 5.76. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80; H, 5.59%.)

The part less soluble in water was recrystallized from methanol. Its melting point was found to be 252–253° and was not lowered by admixture with strychnino one-γ. Thus the identity of the compound with γ-derivative was established.

Catalytic Reduction of Strychninolone-ε. Strychninolone-ε (m.p. 240–243°) was dissolved in alcohol and subjected to reduction in the current of hydrogen gas in the presence of Pd-black. After shaking the mixture for three to four hours, the current of hydrogen gas was stopped and the solution was filtered in order to remove Pd-black. When the filtrate was evaporated, crystals melting at 208–210° were obtained. When they were recrystallized from a large amount of methanol, unchanged strychninolone-ε separated first and dihydro-strychninolone-ε crystallized out next upon further evaporation of the solvent; its melting point was 257°. It was again recrystallized from alcohol and obtained in prisms; the melting point was still 257°. (Found: C, 68.09, 68.29; H, 6.67, 6.77. Calc. for $C_{19}H_{20}N_2O_3 \cdot {}^1/_2H_2O$: C, 68.46; H, 6.30%. Found for dehydrated substance: C, 70.42, 70.44; H, 6.13, 5.99. Calc. for $C_{19}H_{20}N_2O_3$: C, 70.37; H, 6 17%.)

Acetyl-strychninolone-ε. For the preparation of acetyl-strychninolone-ε, the directions given for the preparation of the acetyl derivative of strychninolone-α were followed. It was purified by recrystallization from methanol and ethanol. Needles, m.p. 214–215°. (Found: C, 69.17, 69.27; H, 5.99, 5.82. Calc. for $C_{21}H_{20}N_2O_4$: C, 69.23; H, 5.52%.)

Oxidation of Strychninolone-a with Chromic Acid: Formation of Strychninone. To 3g. of strychninolone, dissolved in 200c.c. of glacial acetic acid, 1.2g. of chromic anhydride, dissolved in 100c.c. of glacical acetic acid, were added little by little with constant stirring. The mixture was allowed to stand overnight and the glacial acetic acid was distilled under reduced pressure. The residue was dissolved in water and shaken with acetic ester. The acetic ester was separated and washed with water. After the removal of the solvent, the residue was treated with a small amount of methanol, and the methanol was evaporated until the odour of acetic acid almost vanished, when a crystalline substance separated out. It was dissolved in a small amount of methanol, filtered, and acetic ester was added to the solution, when crystals melting at 273° were obtained. They dissolve in dilute alkali in slight yellow colour and are reprecipitated with carbon dioxide. (Found: C, 71.39, 71.41; H, 5.37, 5.37. Calc. for $C_{19}H_{16}N_2O_3$: C, 71.25; H, 5.00%.)

Oxidation of Dihydrostrychninolone-a with Chromic Acid. To 2g. of dihydrostrychninolone-a (m.p. 275°), dissolved in glacial acetic acid, 1.0g. of chromic anhydride, dissolved in glacial acetic acid, was added drop by drop. The mixture was allowed to stand overnight and the solvent was distilled under reduced pressure. The residue was treated with water and shaken with acetic ester. The layer of acetic ester was separated, dried with anhydrous sodium sulphate, and when the solvent was distilled, crystals came out. They were recrystallized from acetic ester, m.p. 314°. They dissolve slowly in alkali. (Found: C, 71.25, 71.07; H, 5.61, 6.11. Calc. for $C_{19}H_{18}N_2O_3$: C, 70.80; H, 5.59%.)

INFLUENCES OF HYDROGEN-ACCEPTOR ON FUCOSE FERMENTATION BY ASPERGILLUS ORYZAE.

By Tetsutaro TADOKORO.

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On the mechanism of fucose fermentation, no experimental results have been hitherto reported. It has to be explained by reference to pentose fermentation which has been investigated by some authors. The mechanism of pentose fermentation by fungus is different from that by bacteria. In the latter case, CO_2, acetone, acetic, lactic, and succinic acids, and ethyl alcohol are found in the fermentation products. In the former case it was stated by Behren[1] that *Botrytis cinerea*, *Rhizopus nigricans*, and *Penicillium glaucum* utilized arabinose. It was also stated by Czapek[2] that *Aspergillus niger* consumed xylose and arabinose, though the products are far different from those of fermentation by fungus. Niktinsky reported that *Aspergillus niger* easily utilized arabinose as a carbon source and that there is no difference from *d*-glucose. Peterson, Fred, and Schmidt[3] stated that when pentose, i.e. arabinose, was fermented by *Aspergillus*, by *Penicillium*, or by *Mucor*, they could not find any alcohol nor volatile acid excepting CO_2. White and Willamen[4] reported that *Fusarium* formed alcohol from arabinose. Amelung[5] isolated citric acid from *Aspergillus* culture media containing arabinose. Butkewitsch[6] stated that citric acid was formed from arabinose by *Citromyces* while only a trace was formed by *Aspergillus*. Accordingly the present author has explained the mechanism of arabinose fermentation as follows: arabinose would be broken down to C_3-compound at first and glucose might be changed to glucuronic acid then to saccharic acid and at last to citric acid. Jurist[7] stated that the saccharic acid then changes to ketipinic acid and at last to citric acid while Franzen and Schmidt formed citric acid from ketipinic acid ester, treating with KOH. Tamiya[8] found kojinic acid in the fermentation by *Aspergillus flavus*. Schreyer[9] reported that *Aspergillus*

(1) Behren, *Centr. Bakt.*, II, **4** (1898), 514.
(2) Czapek, *Hofmeister's Beitrage*, **3** (1902), 62.
(3) Peterson, Fred, and Schmidt, *J. Biol. Chem.*, **60** (1924), 628.
(4) White and Willamen, *Biochem. J.*, **22** (1928), 583.
(5) Amelung, *Z. physiol. Chem.*, **166** (1927), 161.
(6) Butkewitsch, *Biochem. Z.*, **142** (1923), 195.
(7) Jurist, *J. Am. Chem. Soc.*, **44** (1925), 1136.
(8) Tamiya, *Acta Phytochim.*, **4** (1929), 227.
(9) Schreyer, *Biochem. Z.*, **202** (1928), 131.

formed fumaric acid from arabinose. There is only one report that methylpentose, i.e. isorhodeose, was fermented by *Aspergillus niger* to form tartaric acid.

Among the yeasts, it was reported by Lintner that *Schizosaccharomyces thermantitonum* ferments arabinose but other kinds of yeast do not. Many yeasts contain large quantities of methylpentosan, which is called yeast gummy substance and the nucleic acid of yeast contains ribose, a kind of pentose.

As to bacteria, it was reported by Schmidt and Peterson[10] that the acetone fermentation bacteria formed butyl alcohol, acetone, volatile and non-volatile acids with CO_2 and by Bertrand[11] that in sorbose fermentation, *Bacterium xylinum* formed arabonic acid. Lafar[12] stated that oxalic acid fermentation was caused by *B. aceti*, *B. acetogenum*, *B. ascendens*, *B. Kutzengianum*, *B. xylinum*, and by *Thermobacter aceti*. Grimbert[13] proved that *Pneumococcus* formed lactic acid and acetic acid from arabinose, Further, Tollens[14] proved that ethyl alcohol is formed by *B. ethaceticus* and by other putrefaction bacteria. Seiler[15] stated that anhydropentose was changed to galactan, $C_{12}H_{20}O_{10}$, by *B. metarabinum* and by *B. persiae*.

Among the references on the influences of the hydrogen acceptor, i.e. oxygen, methyl blue, and quinone, in acetic acid fermentation, Tamiya and Tanaka[16] stated that quinone is the most powerful reagent. Thus the dehydration due to the presence of these reagents in acetic acid fermentation is explained by the following chemical reaction: $CH_3CH_2OH + Acc. = CH_3CHO + H_2Acc.$ or $CH_3CH(OH)_2 + Acc. = CH_3COOH + H_2Acc.$ Also the same reaction was observed in the case of the formation of succinic acid from acetic acid, of fumaric acid and of succinic acid from alcohol and of fumaric acid from succinic acid. Fischer[17] observed fumaric and maleic acid formation from Na-succinate of muscle in the presence of methyl blue. Also there is need of the hydrogen acceptor in the formation of propionic acid from lactic acid and formic acid decomposition to CO_2.

However, there is no report concerning the products of fucose fermentation by *Aspergillus oryzae* nor the differences in the fermentation products when cultured by the same fungus under different conditions of culture.

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(10) Schmidt and Peterson, *J. Biol. Chem.*, **61** (1924), 163.
(11) Bertrand, *Compt. rend.*, **126** (1898), 762.
(12) Lafar, "Handbuch Tech. Mykolog.", Bd. 5, 583.
(13) Grimbert, *Ann. inst. Pasteur*, **9** (1895), 240.
(14) Tollens, *J. Landw.*, **49** (1901), 29.
(15) Seiler, *Centr. Bakt.*, II, **4** (1898), 514.
(16) Tamiya and Tanaka, *Acta Phytochim.*, **6** (1932), 1.
(17) Fischer, *Arch. Pharma.*, **257** (1919), 33.

The writer has had the opportunity of getting plentiful amounts of substances consisting principally of fucose in the experiments relating with chemical studies of *Iridaea laminarioides*.

Preparation of fucose. The air-dried samples of *Iridaea laminarioides*, upon extraction with 35% alcohol at 40°C., yielded a very small amount of viscous liquid containing colouring matters. The evaporated extract was mixed with acetone and the precipitate was freed from acetone and extracted again with alcohol to free it from chromoproteid. The residue was hydrolysed with 5% H_2SO_4, neutralised with $Ba(OH)_2$ and then filtered. The filtrate was evaporated and treated with alcohol to obtain the syrup of sugars. This syrup is made up of the hydrolytic products of the dilute alcohol soluble polysaccharides and the hydrolysed products are composed from fucose. *Aspergillus oryzae* was then cultured at 30°C. for a few days until the time of spore formation. The nutritional salts were prepared as follows: $NaNO_3 = 4$, $KH_2PO_4 = 2$, $MgSO_4 \cdot 7H_2O = 1$, $FeCl_3 = 1$ drop in 100 c.c. of water.

Separation and detection of the fermentation products. The fungus membrane of the surface of the fermented liquid was taken away, the liquid was filtered, and freed from volatile matters by steam distillation. The distillate was used as samples for the detection of acetaldehyde, acetone, alcohol, acetic acid, and formic acid.

The residual liquid was neutralised with NaOH, Cu-acetate was added to precipitate kojinic acid, the liquid filtered, and the filtrate was acidified with acetic acid and then precipitated with Pb-acetate. The Pb-precipitate may contain oxalic, citric, fumaric, tartaric, and allied acids, and when the filtrate is made alkaline with ammonia, the precipitate which is formed by Pb-acetate may contain glycolic acid, and its filtrate, lactic acid. The Pb-precipitate, containing oxalic, citric, and allied acids, was treated with H_2S and reprecipitated with Pb-acetate in 50% alcohol solution in the presence of ammonia. The oxalic acid fraction was insoluble and the citric acid fraction became soluble. The Pb-precipitate, containing citric and tartaric acid fraction was treated with H_2S; then the filtrate was concentrated and mixed with two volumes of 95% alcohol, some K-acetate was added. Then the precipitate was found to be composed of tartaric and the filtrate was citric acid.

For the detection of acetaldehyde, the silver mirror reaction, the phenylhydrazine reaction and the *p*-bromo-phenyhydrazine reaction were employed. For the detection of acetone, Gablielsen's Na-nitroprusside reaction was used with ammonia. For the detection of alcohol, the iodine and K-iodide reactions were carried out with KOH. For the detection of acetic acid, the formation of the hexa-acetate of ferri-salt was used, and also the distillation test of

Ca-acetate and the silver acetate crystals with $AgCO_3$. For the detection of formic acid, the precipitate by Pb-acetate in ammoniacal solution, the colour reaction with $FeCl_3$ and with resorcinol and H_2SO_4, and the detection of methyl blue with K-bisulphite were employed. For the detection of kojinic acid use was made of the colour reaction with $FeCl_3$, the reducing test with Fehling's solution, the diazo-reaction with diazobenzenesulphonic acid, and determination of the melting point. For the detection of lactic acid, the guaiacol reaction with H_2SO_4, the acetaldehyde formation, treatment with K-permanganate and the crystallisation of Zn-lactate were used. For the detection of glycolic acid, the *p*-cresol reaction with acetic acid and H_2SO_4, Bülow's hydrazine reaction with $FeCl_3$ and H_2SO_4, and the crystals and the melting point of the phenylhydrazide were examined. For the detection of citric acid, the formation of Hg-$HgSO_4$, acetone-dicarboxylic acid salt by Denigès's reagent, Stahre's reaction with K-permanganate, and Na-nitroprusside reaction were tested. For the detection of tartaric acid, Fenton's dihydroxymaleic acid reaction, the colour reactions with resorcinol, with *α*-naphthol and with ammonium molybdate were employed. For the detection of fumaric acid, the melting point of free acid and Ca-fumarate was examined. For the detection of oxalic acid, the colour reaction with $FeCl_3$, with resorcinol and H_2SO_4, and the Ca-Ag-oxalate were examined. For the detection of glycerinaldehyde, the orcinol and the phloroglucinol reaction, the reduction of Fehling's solution, and the phenylosazone were examined. For the detection of carboxylic acid, the colour reactions of *α*-naphthol, of phloroglucinol, of orcinol, of resorcinol and of naphthoresorcinol were examined, and the osazone test was made.

Differences between fucose fermentation products by *Aspergillus oryzae* with and without methyl blue. The liquid resulting from fermentation of fucose by *Aspergillus oryzae* with and without methyl blue, was filtered, and distilled in steam. Both the distillates showed neither the acetaldehyde reactions, i.e. the phenylhydrazine or the silver mirror reaction, nor acetone reaction, i.e. reaction with Na-nitroprusside, acetic acid, and ammonia. The filtrate showed also no alcohol reaction, i.e. reaction with KI, iodine, and KOH, and no acetic acid reaction, i.e. with $FeCl_3$. These results coincide with the results of tests of the distillate of arabinose fermentation which were reported in the Journal of Agr. Chemical Society of Japan.[18]

As to the detection of formic acid by means of Pb-acetate, and $FeCl_3$, and by resorcinol and H_2SO_4, the reactions were faint, and in the presence of methyl blue, these reactions were not observed at all, while as to the arabinose fermentation, pretty noticeable reactions were observed.

(18) Tadokoro, *J. Agr. Chem. Soc. Japan*, **11** (1935), 167.

The distillation residue was neutralized with NaOH and a precipitate was formed, Cu-acetate added, the liquid filtered, the filtrate was freed from Cu-salts, and the Pb-precipitate was formed by Pb-acetate after acidification with acetic acid. In the detection of kojinic acid obtained from H_2S decomposition of Cu-precipitates, the $FeCl_3$ reaction, the reduction of Fehling's solution, and the diazo-reaction, were positive, although, when it was extracted with ether, no crystals could be obtained; but when methyl blue was used, no reaction could be observed.

The Pb-precipitate which corresponds to the oxalic and citric acid fraction, was obtained as stated above by the treatment with Pb-acetate and acetic acid. From the filtrate, after making it alkaline with ammonia, the Pb-precipitate was obtained, which corresponds to the glycolic acid fraction. After the separation of this precipitate, the filtrate contained also Pb-salts which correspond to the lactic acid fraction.

The Pb-precipitate of the oxalic acid and citric acid fraction was decomposed with H_2S, and after being concentrated, Pb-acetate and ammonia were added in the presence of 50% alcohol. Therefore the oxalic acid fraction comes out as precipitate while the citric acid fraction remains in the filtrate. All these Pb-salts were decomposed with H_2S, filtered, the filtrate was concentrated and the various reactions were examined.

For the detection of glycolic acid, the concentrated solution was treated with ether. After the ether extract was freed from ether, the following reactions were tested. The cresol reaction with glacial acetic acid and H_2SO_4 showed greenish blue and the guaiacol reaction showed violet colour. Bülow's reaction[19] with $FeCl_3$ and H_2SO_4 in the presence of phenylhydrazine showed reddish violet. The phyenylhydrazone was formed, treated with phenylhydrazine on the water bath, freed from the excess of phenylhydrazine, extracted with ether, and white crystals of the phenylhydrazide were obtained which melted at 118°C. after purification with acetic acid. But in the case of using methyl blue, these colour reactions were not observed at all.

For the detection of lactic acid and maleic acid, after the concentrated solution was treated with ether, examination was made of the following reaction.

As to the formation of acetaldehyde, upon heating the solution with K-permanganate it was detected. The rose colour was also observed after treating with H_2SO_4 and guaiactincture, and bright yellow was seen with $FeCl_3$. A large quantity of the liquid was boiled with $ZnCO_3$, and crystals of Zn-lactate were obtained. When the ZnO content was determined by the ordinary method, it was found to correspond to 28.02%. But in the case of

(19) Bülow, *Ann.*, **236** (1886), 195.

using methyl blue, these reactions were not observed and naphthoresorcinol reaction only was seen. Further for the detection of maleic acid, Denigès's reaction[20] and diazo-reaction were observed, but Kleeman's reaction could not be observed. From these results in the case of using methyl blue, maleic acid is apparently formed instead of lactic acid.

For the detection of oxalic acid, the precipitate with $CaCl_2$ in ammoniacal solution which is insoluble in acetic acid was formed. The resorcinol H_2SO_4 reaction showed green blue, the $FeCl_3$ reaction showed greenish yellow. But Cu-oxalate with Cu-acetate, and Ag-oxalate with $AgNO_3$ were formed in small quantities in the presence of HNO_3, so the liquid does not seem to contain large quantities of oxalic acid.

In the detection of citric acid, the white precipitate with Denigès's reagent and the characteristic colour with Na-nitroprusside were not observed, so the presence of citric acid is questionable. For the detection of tartaric acid, Fenton's reaction with $FeSO_4$ and H_2O_2 and the ammonium molybdate reaction with H_2O_2 were negative. Therefore the presence of tartaric acid is also uncertain. The resorcinol H_2SO_4 and the α-naphthol-H_2SO_4 reactions which are common to this acid and succinic acid were observed. But the pyrrole-reaction of succinic acid was very faint, and in the $FeCl_3$ reaction no precipitate was formed, but the material showed only a clear red colour. From these results it may be stated that the presence of succinic acid is questionable while that of oxocarboxylic acid is more probable. Further, in the phloroglucinol-HCl and in the orcinol-HCl reactions, the red colour was indicated in amyl alcohol, and the reddish violet colour was indicated in ether in the naphtho-resorcinol-HCl reaction. The oxocarboxylic acid not precipitated by Cu-acetate, did not give the diazo-reaction and did not reduce Fehling's solution; those points are distinguished from kojinic acid. This acid formed osazone with phenylhydrazine and acetic acid, it is soluble in ether and melts at 155–158°, so it is near to the melting point of glucuronic acid. In the case of using methyl blue, it gave a strong diazo-reaction, so it is probable that maleic acid is formed in the fermented liquid.

The lactic acid fraction was extracted with ether, and the extract freed from ether. It showed red colour when tested with orcinol, with phloro-glucinol and H_2SO_4, and also with resorcinol and HCl, so it seems to contain glycerinaldehyde.

Differences in chemical mechanism of fucose fermentations with and without methyl blue. Recently Peterson and Fred[21] observed the formation of lactic and acetic acids in the heterogeneous lactic acid fermentation of

(20) Denigès, *Compt. rend.*, **130** (1900), 32.
(21) Peterson and Fred, *J. Biol. Chem.*, **64** (1925), 643.

xylose by *Lactobacillus pentaaceticus* and also of arabinose by *Pneumococcus* as stated above. As it has already been stated by Virtanen[22] that the preform of lactic acid is methylglyoxal hydrate in sugar fermentation by *B. coli*, this mechanism will be assumed in the following methylpentose fermentation. Years ago Tates[23] stated that lactic acid formation was observed in the fermentation of rhamnose by *Friedlander's bacillus*, and the other report stated also that isorhodeose was fermented by certain microorganisms. In the case of methylpentose fermentation, the glycolic acid formation was observed always remarkably, so the chemical mechanism of other acid formation may be communicated to this acid. For example, it was stated by Challenger that formic acid was formed from glycolic acid in oxidative fermentation by *Aspergillus niger*.

Butkewitsch[24] stated that citric acid is formed always from glycolic acid by condensation. Fedorff proved the formic acid and the acetaldehyde formation from methylglyoxal by bacteria, and Sakaguchi proved that citric acid is formed easily from acetaldehyde by *Aspergillus* as had already been stated by Neuberg. Tamiya[16] stated that citric acid is formed from two mols of acetic acid and one mol of formic acid.

The acetaldehyde might be formed from methylglyoxal by the dehydration process. In the condensation of acetaldehyde, oxalacetic acid is formed at first, and then maleic acid might be formed also. The maleic acid formation in hexose fermentation was proved by Nishikawa, with cultured *Aspergillus*. Aubel[25] stated following Quastel's explanation that by oxidation, propionic, acetic, and formic acids are formed while by dehydration, fumaric, maleic, and lactic acids are formed from succinic acid in sugar fermentation.

Sumiki[26] proved that the maleic acid formation with other organic acids occurs in the hexose fermentation by *Aspergillus glaucus*.

In the fucose fermentation, the presence of glycerinaldehyde was proved in the experiment as the intermediate product, so kojinic acid was assumed to be formed from glycerinaldehyde by the oxidative synthesis as stated by Tamiya, and the citric acid is formed by the condensation of glycerinaldehyde as stated by Sakaguchi.

The presence of oxocarboxylic acid in the sugar fermentation liquid was reported by Butkewitsch who stated that bacteria formed glucuronic acid from

(22) Virtanen, *Ann. acad. sci. Fennicae*, **29** (1927), No. 26.
(23) Tates, Czapek's "Biochem. d. Pflanzen", I, 1913, 316.
(24) Butkewitsch, *Biochem. Z.*, **142** (1923), 195.
(25) Aubel, *Ergebnisse d. Enzymforschung*, **4** (1935), 251.
(26) Sumiki, *J. Agr. Chem. Soc. Japan*, **6** (1930), 1153; **7** (1931), 819.

gluconic acid. According to Sumiki the latter is proved in the oxidative fermentation of hexose by *Aspergillus*. In the same way, it was stated by Tamiya that arabonic acid is formed in arabinose fermentation by *Aspergillus flavus*, and also by Bertrand that the same acid formation is caused by *Bacterium xylinum*. Next, Sumiki[26] proved 2-hydroxymethylfurane-5-carboxylic acid formation in the hexose fermentation by *Aspergillus glaucus* and gluconic acid formation by other *Aspergillus*. Further Sakaguchi proved gluconic acid formation from glycerine by *Aspergillus*, so it shows that the gluconic acid formation is not only a result of the simple oxidation of glucose but it is caused by the oxidative synthesis from the substances with smaller molecules. Therefore, it is probably formed from pentose and methylpentose and also from their cleavage products. The author found glycerinaldehyde which comes easily from glycerine by dehydration in the fucose fermented liquid, and it is more likely that glycerinaldehyde forms gluconic acid and then oxocarboxylic acid.

Anyhow, the important fact of chemism in the cleavage of pentose molecule is the formation of C_3- and C_2-compound as stated by Lek[27] that in butyl alcohol fermentation by bacteria, the first cleavage of pentose molecule occurs to form an equimolecular mixture of methylglyoxal and glycoaldehyde.

In the above explanation, the author intended to consider the influences of the hydrogen acceptor in the light of the experimental results reported in the above section.

As described in the above section, the influences of methyl blue on acetic acid fermentation caused acetaldehyde to be formed from ethyleneglycol, etc. In muscle there is formed also maleic acid from succinic acid, etc. And it is known that the dehydration reaction of yeast[23] is greatly retarded in the presence of methyl blue and their cleavage mechanism is prevented, so much quantities of acetaldehyde were found instead of alcohol, caused by delay in the dismutation of acetaldehyde to alcohol. For the same reason, the action of yeast on methylglyoxal and on pyroracemic acid is always delayed. It is known that various changes were wrought upon chemism of fermentation by the presence of sulphite such as the accumulation of acetaldehyde in alcohol fermentation and in butyric acid fermentation, and such as that of pyroracemic acid in propionic acid fermentation of glucose.

In fucose fermentation with methyl blue, the formic acid formation was delayed, and this change of chemical mechanism is caused by the prevention of the oxidation and of the dehydration of these acid forming substances. So the prevention of the following chemical mechanisms happens as stated by

(27) Lek, Diss. Delft, 1930.

(28) Sonderhoff, *Ergebnisse d. Enzymforschung*, **3** (1934), 183.

many authors in the different cases of fermentation, for instance, by Harden, by Grey, by Neuberg and by Scheffer in hexose fermentation by *B. coli*:

$C_6H_{12}O_6 + H_2O \rightarrow CH_3COOH + CH_3CH_2OH + 2HCOOH$ (Harden);
$CH_3COCHO \rightarrow HCOOH + CH_3CHO$ (Grey);
$RCOCOOH + H_2O \rightarrow RCOOH + HCOOH$ (Neuberg);
$C_6H_{12}O_6 \rightarrow 2C_3H_6O_3$, $CH_3COCH(OH)_2 \rightarrow CH_3CHO + HCOOH$ (Scheffer).

The last reaction is also stated to occur in hexose fermentation by *B. Aerogenes*. Brinkmann stated the following reaction in anaerobic culture of lower fungus:

$$2CH_2COCOOH \rightarrow COOHCOCH_2CH_2COOH + 2H_2O \rightarrow HCOOH + COOHCH_2CH_2COOH.$$

By Challenger the following reaction was stated in the culture media of *Aspergillus niger*: $CH_2OHCOOH \rightarrow HCOOH + H_2O + CO_2$.

Thus the formation of CO_2 and H_2 from formic acid is caused by dehydration, and these reactions must be delayed also as less CO_2-formation was observed in the experimental results.

Aubel stated that in the oxidative fermentation of hexose by *Aspergillus*, propionic, acetic, and formic acids were formed, while in the case of the prevention of oxidation, fumaric, maleic, and lactic acids were formed by dehydration and also maleic acid formation was observed from lactic acid. So in the experiment of the fucose fermentation, using methyl blue, maleic acid would be observed instead of formic acid which is formed in the case of fermentation without methyl blue. The following lactic acid formation is also prevented by using methyl blue in the fucose fermentation:

$$CH_3COCHO \rightarrow CH_3CHOHCOOH.$$

Glycolic acid is a normal product in the fucose fermentation by *Aspergillus oryzae* but it could not be detected under the influence of the addition of methyl blue, so the following reaction would be prevented:

$CH_3COOH \rightarrow CH_2OHCOOH \rightarrow HCOOH + H_2O + CO_2$;
$CH_2OHCHO \rightarrow CH_2OHCOOH$.

NEW COMPOUNDS OF UREA-FORMALDEHYDE CONDENSATION PRODUCTS.

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Although many reports concerning urea-formaldehyde condensation products have been published by many investigators since Hölzer[1], of these condensation products, there are only two whose constitutional formulae have been accounted for to this day. They are namely, monomethylol-urea[2] (H_2N–CO–NH–CH_2OH) and dimethylol-urea[3] ($HOCH_2$–NH–CO–NH–CH_2OH). They are soluble crystalline compounds. It has been observed that urea-formaldehyde condensation products contain, besides crystalline compounds, insoluble amorphous compounds and resinous compounds. Of these, resinous compound is so-called urea resin, and is also termed "organic glass,"[4] being one of the important synthetic resins. The present author[5] has, for the past few years, been investigating methods of manufacture of this resin, and especially, most recently, investigated the chemical constitution and the mechanism of formation of this resin and fortunately succeeded in obtaining the expected results.

In this paper the author wishes to report on the thirty new compounds (given in Table 1) out of the condensation products of urea or urea derivatives with formaldehyde, which the author succeeded in synthesizing in the course of his research.

Methylenediurea (I, Table 1) was obtained, in the presence of acid, by the action of 1 mol of formaldehyde on 8 mol of urea. In the past, in the production of urea-formaldehyde condensation products, we had some instances in which formaldehyde was used as (raw) material considerably in excess. However, in the case of urea, 1.33 mol of urea on 1 mol of formaldehyde, as used by Dixon[6], was the maximum, and the use of any greater excess has never been reported. But the present author succeeded in obtaining methylenediurea as the result of experiment with a great excess of urea as (raw) material. Generally speaking, when urea is reacted upon formaldehyde in

(1) Hölzer, *Ber.*, **17** (1884), 659.
(2) (3) Einhorn and Hamburger, *Ber.*, **41** (1908), 21.
(4) There are other names besides "organic glass."
(5) Kadowaki, *Repts. Imp. Ind. Research Laboratory, Osaka, Japan*, **7** (1926), No. 6; **13** (1932), No. 3, No. 6; **14** (1933), No. 6; **14** (1934), No. 11; **16** (1935), No. 6.
(6) Dixon, *J. Chem. Soc.*, **113** (1918), 233.

Table 1.

No.	Name	Constitutional formula	Properties	Photogram
I	Methylene-diurea	$H_2C(NH-CO-NH_2)_2$	Needle-crystals m.p. 218°C. (effervesces)	Fig. 1 500×
II	Trimethylene-tetraurea	$H_2C(NH-CO-NH_2)(NH-CO-NH)CH_2(NH-CO-NH)(NH-CO-NH_2)$	White powder, at 230°C. turns yellow.	Fig. 2 500×
III	Penta-methylene-hexaurea	$H_2C(NH-CO-NH_2)(NH-CO-NH)CH_2(NH-CO-NH)(NH-CO-NH)CH_2(NH-CO-NH)(NH-CO-NH_2)$	White powder, at 236°C. turns yellow.	Fig. 3 500×
IV	Methylol-methylene-diurea	$H_2C(NH-CO-NH_2)(NH-CO-NH-CH_2OH)$	White powder.	Fig. 4 500×
V	Methylenebis-methylolurea	$H_2C(NH-CO-NH-CH_2OH)_2$	White powder m.p. 228°C. (effervesces)	Fig. 5 500×
VI	Methylenebis-acetylurea	$H_2C(NH-CO-NH-COCH_3)_2$	Needle-crystals m.p. 156°C.	Fig. 6 20×
VII	Methylenebis-methylurea	$H_2C(NH-CO-NH-CH_3)_2$	Prism-crystals m.p. 184°C.	Fig. 7 20×
VIII	Mono-methylolurea-methylether	$OC(NH-CH_2-OCH_3)(NH_2)$	Plate-crystals m.p. 91°C.	Fig. 8 16×
IX	Mono-methylolurea-ethylether	$OC(NH-CH_2-OC_2H_5)(NH_2)$	Needle-crystals m.p. 111°C.	Fig. 9 40×
X	Dimethylolurea-dimethylether	$OC(NH-CH_2-OCH_3)_2$	Needle-crystals m.p. 101°C.	Fig. 10 40×
XI	Dimethylolurea-diethylether	$OC(NH-CH_2-OC_2H_5)_2$	Plate-crystals m.p. 124°C.	Fig. 11 40×

Table 1. (*Continued*)

No.	Name	Constitutional formula	Properties	Photogram
XII	Dimethylolurea-di-*n*-propylether	$OC(NH-CH_2-OC_3H_7)_2$	Prism-crystals m.p. 95°C.	Fig. 12 57.5×
XIII	Dimethylolurea-di-*n*-butylether	$OC(NH-CH_2-OC_4H_9)_2$	Needle-crystals m.p. 93°C.	Fig. 13 40×
XIV	Dimethylolurea-di-*n*-amylether	$OC(NH-CH_2-OC_5H_{11})_2$	Plate-crystals m.p. 84°C.	Fig. 14 80×
XV	Dimethylolurea-dibenzylether	$OC(NH-CH_2-OCH_2C_6H_5)_2$	Needle-crystals m.p. 112°C.	Fig. 15 57.5×
XVI	Dimethylolurea-diethylthioether	$OC(NH-CH_2-SC_2H_5)_2$	Pillar-crystals m.p. 108.5°C.	Fig. 16 30×
XVII	Methylenebis-methylolurea-methylether	$H_2C(NH-CO-NH-CH_2-OCH_3)_2$	Plate-crystals, at 240°C. turns yellow.	Fig. 17 30×
XVIII	Dimethyloltri-methylene-tetraurea-dimethylether	$H_2C(NH-CO-NH-CH_2-OCH_3)(NH-CO-NH)_2CH_2$	White powder.	
XIX	Monomethylol-urea peroxide	$OC(NH-CH_2-O-OH)(NH_2)$	Needle-crystals m.p. 153°C.	
XX	Hexamethylol-triurea peroxide	$HO-O-CH_2-NH-CO-NH-CH_2-O-CH_2-NH-CO-NH-CH_2-O-CH_2-NH-CO-NH-CH_2-O-OH$	Amorphous powder.	
XXI	*N,N'*-Dimethylol-urondimethyl-ether	$CH_3O-CH_2-N(CO)N-CH_2-OCH_3$, H_2C, CH_2, O	Colourless transparent liquid, b.p. 82–83°C. (0.1 mm.)	
XXII	*N,N'*-Dimethylol-urondiethyl-thioether	$C_2H_5S-CH_2-N(CO)N-CH_2-SC_2H_5$, H_2C, CH_2, O	Pillar-crystals m.p. 59°C.	Fig. 19 20×

Table 1. (*Concluded*)

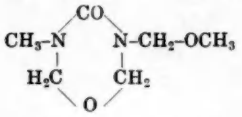
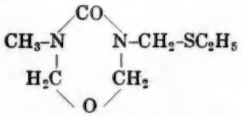
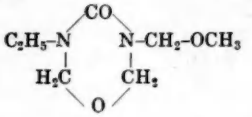
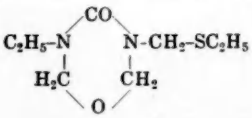
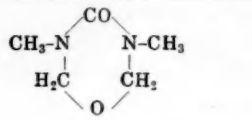
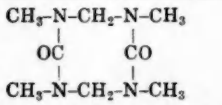
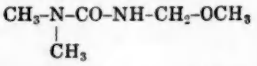
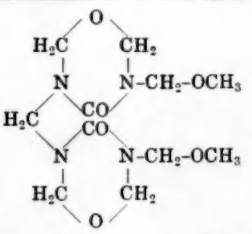
No.	Name	Constitutional formula	Properties	Photogram
XXIII	*N*-Methyl-*N'*-methyloluron-methylether		Colourless transparent liquid, b.p. 89–90°C. (0.2 mm.)	
XXIV	*N*-Methyl-*N'*-methyloluron-ethylthioether		Colourless transparent liquid, b.p. 122–125°C. (1.0 mm.)	
XXV	*N*-Ethyl *N'*-methyloluron-methylether		Colourless transparent liquid, b.p. 91–93°C. (1.0 mm)	
XXVI	*N*-Ethyl-*N'*-methyloluron-ethylthioether		Needle-crystals m.p. 15.5°C.	
XXVII	*N,N'*-Dimethyl-uron		Prism-crystals m.p. 38.5°C.	
XXVIII	Tetramethyl-dimethylene-diureid		Needle-crystals m.p. 258°C.	Fig. 20 40×
XXIX	*N,N*-Dimethyl-*N'*-methylolurea-methylether		Prism-crystals m.p. 65°C.	
XXX	Methylenebis-methyloluron-methylether		Colourless transparent sticky substance.	

Fig. 1.

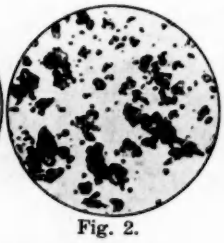


Fig. 2.

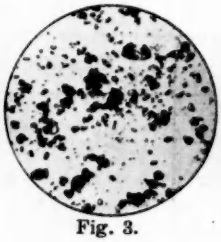


Fig. 3.

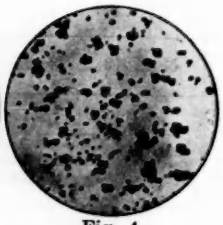


Fig. 4.

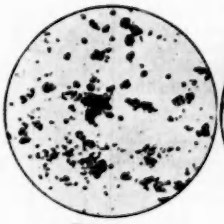


Fig. 5.

Fig. 6.

Fig. 7.

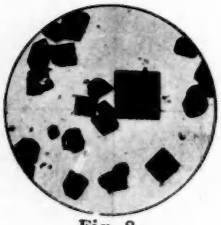


Fig. 8.

Fig. 9.

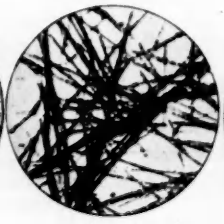


Fig. 10.

Fig. 11.

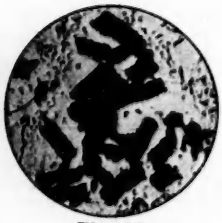


Fig. 12.

Fig. 13.

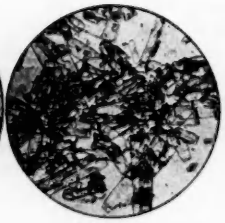


Fig. 14.

Fig. 15.

Fig. 16.

Fig. 17.

Fig. 18.

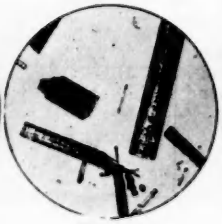


Fig. 19.

Fig. 20.

the presence of acid, there is a strong tendency to form polymer, and as the existence of acid is necessary for the formation of methyleneurea in water solution, if lower methyleneurea alone is desired to be obtained, special conditions of experiment must be prepared. According to the author's observation, insoluble methyleneurea[7] heretofore known, should be regarded as the mixture of higher methyleneurea.

It is noteworthy that such a soluble crystalline methyleneurea as methylenediurea was obtained, while methyleneurea heretofore known is insoluble. The author, by taking advantage of the solubility of methylenediurea, was enabled to know the nature and the formation characteristics[8] of methyleneurea, and consequently was able to know also the formation characteristics[9] of methylolurea. This new knowledge of the formation characteristics of methyleneurea and methylolurea would surely be most useful in the manufacture of resin.

In the next place trimethylenetetraurea (II) and pentamethylenehexaurea (III) were obtained in the following method: The precipitate which was formed by the addition of a small quantity of acid to the aqueous solution of methylenediurea, was subjected to a fractional extraction by means of hot water and boiling water, and each was obtained as the precipitate from the extract. These are interesting compounds for the purpose of observation of the constitution of the higher methyleneurea.

Methylolmethylenediurea (IV) and methylenebismethylolurea (V) were obtained, by the action of formaldehyde, in the presence of alkali, upon methylenediurea. Of these, compound V yields colourless, transparent, hard resin when it is heated under pressure. This resin is highly water-proof, and does not crack even when it is soaked in boiling water for several hours. Since, up to this time, the defect of urea-resin for practical use has been its lack of water-proof quality, it is noteworthy that a kind of resin with water-proof quality in a high degree, was obtained.

Methylenebisacetylurea (VI) was obtained by acetylation of methylenediurea, using acetic anhydride.

Methylenebismethylurea (VII) was obtained by the action of 1 mol of formaldehyde on 2 mol of methylurea (in the presence of acid). Since, in the

(7) Hölzer, *Ber.*, **17** (1884), 659; **18** (1885), 3302 (Anm.). Lüdy, *Monatsh.*, **10** (1889), 297. Hemmelmayer, *Monatsh.*, **12** (1891), 94. Tollens, *Ber.*, **29** (1896), 2751. Dixon, *J. Chem. Soc.*, **113** (1918), 233. Scheibler, Trostler und Scholz, *Z. angew. Chem.*, **41** (1928), 1305.

(8) Kadowaki, *Repts. Imp. Ind. Research Laboratory, Osaka, Japan*, **13** (1932), No. 6, 15–41.

(9) Kadowaki, *ibid.*, **14** (1933), No. 6, 16–29.

case of methylurea, one of the hydrogen atoms of amido-radical of urea has been replaced by a methyl-radical, condensation products formed by the reaction with formaldehyde is considerably simpler, compared with the case of urea.

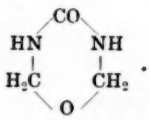
Monomethylolureamethylether (VIII) was obtained by making methyl alcohol act upon monomethylolurea, in the presence of acid. Again, this compound can be obtained simply by heating monomethylolurea with methyl alcohol somewhat longer. So far as the present author knows no research has been made concerning the reaction of alcohol upon monomethylhlurea and dimethylolurea. The author experimented upon the reaction of monomethylolurea, dimethylolurea and methylenebismethylolurea on alcohol or mercaptane, for the purpose of investigating the character of methylolurea, and by using the similar method as used in obtaining the compound VIII, succeeded to obtain compounds from IX to XVII. Of these, compounds formed by the reaction of dimethylolurea upon alcohol yields, on heating, colourless, transparent, hard resin. Above all, resins obtained from XIII, XIV, and XV have been observed to possess a greater degree of water-proof quality.

Next, dimethyloltrimethylenetetraureadimethylether (XVIII) was obtained as precipitate by the action of 8 mol of formalin, in the presence of acid, on 1 mol of urea at about −5°C. On this occasion, the formation of methylether was due to the reaction of methyl alcohol contained in formalin.

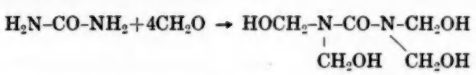
Monomethylolurea peroxide (XIX) and hexamethyloltriurea peroxide (XX) were obtained by the reaction of hydrogen peroxide (slightly acidic to litmus) on monomethylolurea and dimethylolurea. Moreover, the author obtained a liquid peroxide by using hydrogen peroxide which was neutralized beforehand. The author also obtained an insoluble crystalline peroxide $(C_3H_6N_2O_3)_n$ (Fig. 18) by adding acid to the mixture of dimethylolurea and hydrogen peroxide. The above-mentioned crystalline peroxide is different in its process of preparation from those which have been formerly obtained, but as its characteristics and analytical results are alike, it must be related to them.[10]

N,N'-Dimethylolurondimethylether (XXI) was obtained, first by the action of 1 mol of urea on 4 mol of formaldehyde, by heating in the presence of alkali (or by the reaction through concentration at room temperature), and then, by the action of methyl alcohol in the presence of acid. This compound contains, in its constitution, one dimethyleneetherurea-ring. Although this ring is an important one, frequently appearing in urea-formaldehyde condensation products, it is an unknown ring. Therefore, the author gave the name

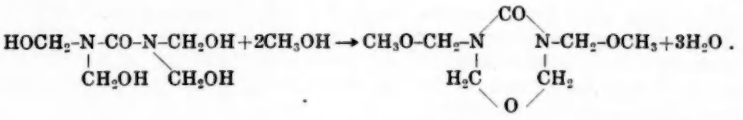
(10) Girsewald and Siegens, *Ber.*, **47** (1914), 2464. Bois de Chesne, *Kolloid Beihefte*, **36** (1932), 418.

of "uron" to the normal constitution of this ring  . This uron ring is a stable ring and does not easily decompose when it is acted on by dilute acid.

That which is formed by the reaction of urea on formaldehyde by heating, first in the presence of alkali, in the process of manufacture of compound XXI is undoubtedly tetramethylolurea:



That the compound XXI was formed in the treatment with methyl alcohol in the presence of acid, could be considered due to the process that, out of the two methylol-radical which were united with each urea amido-radical, one first reacting upon methyl alcohol, formed methylether, and then the other, mutually reacting, formed uron ring:



N-Methyl-*N'*-methyloluronmethylether (XXIII), *N*-ethyl-*N'*-methyloluronmethylether (XXV), *N,N'*-dimethyluron (XXVII)[11], tetramethyldimethylenediureid (XXVIII)[12], *N,N'*-dimethyl-*N'*-methylolureamethylether (XXIX) and methylenebismethyloluronmethylether (XXX) were obtained by the similar method as used in obtaining compound XXI, by the use of methylurea, ethylurea, *N,N'*-dimethylurea, *N,N*-dimethylurea and methylenediurea, in place of urea. All these are compounds whose three or four hydrogen atoms of urea-amidoradical are replaced by methylene-radical or alkyl-radical, and they have a very important place in our observation of the conditions of the union of urea with formaldehyde.

N,N'-Dimethylolurondiethylthioether (XXII) was obtained by the action of ethylmercaptane in the presence of acid on compound XXI. *N*-Methyl-*N'*-methyloluronethylthioether (XXIV) and *N*-ethyl-*N'*-methyloluronethylthioether (XXVI) were obtained by the action of ethylmercaptane, in the presence of acid, on compound XXIII and compound XXV.

(11) (12) *N,N'*-Dimethyluron and tetramethyldimethylenediureid can also be obtained simply by the reaction of *N,N'*-dimethylurea and formaldehyde through heating in the presence of acid.

Experimental.

(1) **Methylenediurea** $C_3H_8N_4O_2$. Urea (1540 g.) was dissolved in the equal weight of water. When 22.5 c.c. of conc. hydrochloric acid and 250 c.c. of 38.37% formalin were added some white turbidity appeared in a few minutes. After leaving the mixture to stand for two days, it was neutralized with potassium hydroxide, and the precipitate from it was scooped out. The precipitate was treated with alcohol, and after urea contained in it was removed, it was recrystallised from water. (Yield: 279.6 g. Found: C, 26.89; H, 6.21; N, 41.98%; mol. wt., 117.6; CH_2O, 23.24%. Calculated for $C_3H_8N_4O_2$: C, 27.25; H, 6.12; N, 42.42%; mol. wt., 132. Calculated for $CH_2O/C_3H_8N_4O_2$: CH_2O, 22.73%.)

(2) **Trimethylenetetraurea** $C_7H_{16}N_8O_4$ **and Pentamethylenehexaurea** $C_{11}H_{24}N_{12}O_6$. Methylenediurea (10 g.) was dissolved in 200 c.c. of water, and when one drop of conc. hydrochloric acid was added to the solution, white turbidity appeared after a few minutes. After leaving the solution to stand for one day, the precipitate was scooped out and was thoroughly washed with water, and then was heated together with 1 l. of water at 95°C., and the solution was filtered while still warm, and when the filtrate was cooled, precipitate was separated. (Yield: 2.97 g. Found: C, 30.52; H, 6.00; N, 40.72; CH_2O, 31.78. Calculated for $C_7H_{16}N_8O_4$: C, 30.41; H, 5.84; N, 40.59. Calculated for $3CH_2O/C_7H_{16}N_8O_4$: CH_2O, 32.61%.) Then, the residue, together with 1 l. of water, was boiled, and was filtered while still warm, and when the filtrate was cooled, precipitate separated out. (Yield: 0.71 g. Found: C, 31.26; H, 5.90; N, 40.11; CH_2O, 34.17. Calculated for $C_{11}H_{24}N_{12}O_6$: C, 31.41; H, 5.76; N, 40.00. Calculated for $5CH_2O/C_{11}H_{24}N_{12}O_6$: CH_2O, 35.71%.)

(3) **Methylolmethylenediurea** $C_4H_{10}N_4O_3$. Methylenediurea (5 g.) was dissolved in 150 c.c. of water, and 0.1 g. of barium hydroxide and 2.96 g. of 38.37% formalin were added to the solution, and after leaving it to stand for 55 minutes, it was neutralized by passing a current of carbon dioxide and was filtered. The filtrate was evaporated and dried. The dried substance was extracted by heating with 60% alcohol. Then, this extract separated out a precipitate when it was cooled. This precipitate contains a small quantity of methylenebismethylolurea. (Yield: 0.58 g. Found: C, 30.57; H, 6.30; N, 32.72. Calculated for $C_4H_{10}N_4O_3$: C, 29.63; H, 6.22; N, 34.59%.)

(4) **Methylenebismethylolurea** $C_5H_{12}N_4O_4$. Methylenediurea (10 g.) was dissolved in 200 c.c. of water and 0.4 g. of barium hydroxide and 11.9 g. of 38.37% formalin were added, and the solution was left to stand for ten minutes, and then, it was neutralized by passing a current of carbon dioxide, and filtered. The filtrate was evaporated and dried. This dried substance was heated with 60% alcohol. The extract separated out precipitate when it was left to cool. (Yield: 2.9 g. Found: C, 31.79; H, 6.25; N, 30.10. Calculated for $C_5H_{12}N_4O_4$: C, 31.23; H, 6.30; N, 29.17%.)

(5) **Methylenebisacetylurea** $C_7H_{12}N_4O_4$. To 6 g. of methylenediurea 20 c.c. of acetic acid, 70 c.c. of acetic anhydride, and 1.5 c.c. of conc. sulphuric acid were added, and when the solution was left to cool after it was boiled for ten minutes, crystals were separated out. The crystals were scooped out, and were recrystallized from water. (Yield: crude 2.4 g. Found: CH_3CO, 59.3. Calculated for $CH_3CO_2H/C_7H_{12}N_4O_4$: CH_3CO, 55.5%.)

(6) **Methylenebismethylurea** $C_5H_{12}N_4O_2$. Methylurea (5.64 g.) was dissolved in 3 c.c. of 37.57% formalin and when one drop of conc. hydrochloric acid was added, the solution generated intense heat, and its temperature rose. When left to cool, crystals were separated out. These crystals were scooped out, and were recrystallized from alcohol. (Yield: crude 4.55 g. Found: N, 35.16. Calculated for $C_5H_{12}N_4O_2$: N, 35.00%.)

(7) **Monomethylolureamethylether** $C_3H_8N_2O_2$. Methyl alcohol (5 g.) and one drop of 5 N hydrochloric acid were added to 0.85 g. of monomethylolurea and were dissolved, and after allowing the solution to stand for one minute, it was neutralized with silver carbonate, and was filtered, and when the filtrate was evaporated, there remained crystals. These crystals were recrystallized from methyl alcohol. (Yield: crude 0.96 g. Found: C, 34.75; H, 7.58; N, 26.94. Calculated for $C_3H_8N_2O_2$: C, 34.58; H, 7.76; N, 26.91%.)

(8) **Monomethylolureaethylether** $C_4H_{10}N_2O_2$. Ethyl alcohol (15 g.) and 3 drops of 5 N hydrochloric acid were added to 1.9 g. of monomethylolurea and were dissolved. After leaving the solution to stand for 7 minutes, it was neutralized with silver carbonate, and was filtered. When this filtrate was concentrated, crystals separated out. These crystals were recrystallized from alcohol. (Yield: crude 1.37 g. Found: N, 23.84. Calculated for $C_4H_{10}N_2O_2$: N, 23.72%.)

(9) **Dimethylolureadimethylether** $C_5H_{12}N_2O_3$. Methyl alcohol (100 c.c.) and one drop of 5 N hydrochloric acid were added to 10 g. of dimethylolurea, and were dissolved, and the solution was left to stand for 5 minutes, and then, it was neutralized with silver carbonate, and was filtered. When the filtrate was concentrated, crystals separated out. The crystals were scooped out and were recrystallized from methyl alcohol. (Yield: 10.6 g. Found: C, 40.36; H, 8.33; N, 19.13%; mol. wt., 138; CH_2O, 40.61%. Calculated for $C_5H_{12}N_2O_3$: C, 40.51; H, 8.17; N, 18.91%; mol. wt., 148. Calculated for $2CH_2O/C_5H_{12}N_2O_3$: CH_2O, 40.54%.)

(10) **Dimethylolureadiethylether** $C_7H_{16}N_2O_3$. Ethyl alcohol (100 c.c.) and one drop of 5 N hydrochloric acid were added to 10 g. of dimethylolurea, and were dissolved. After allowing the solution to stand for 7 minutes, it was neutralized with silver carbonate and was filtered. When the filtrate was evaporated crystals remained. These crystals were recrystallized from alcohol. (Yield: crude 11.9 g. Found: N, 15.96; CH_2O, 34.83. Calculated for $C_7H_{16}N_2O_3$: N, 15.90. Calculated for $2CH_2O/C_7H_{16}N_2O_3$: CH_2O, 34.83%.)

(11) **Dimethylolureadi-*n*-propylether** $C_9H_{20}N_2O_3$. Dimethylolurea (1 g.) was dissolved by the addition of 5 g. of *n*-propyl alcohol and one drop of N hydrochloric acid. After leaving the solution to stand for 10 minutes, it was neutralized with silver carbonate, and was filtered. Through the concentration of the filtrate, crystals separated out. The crystals were scooped out and were recrystallized from ether. (Yield: crude 1.45 g. Found: N, 13.92. Calculated for $C_9H_{20}N_2O_3$: N, 13.72%.)

(12) **Dimethylolureadi-*n*-butylether** $C_{11}H_{24}N_2O_3$. Dimethylolurea (1 g.) was dissolved by the addition of 5 g. of *n*-butyl alcohol and one drop of N hydrochloric acid. After the solution was left to stand for 20 minutes, it was neutralized with silver carbonate, and was filtered. The filtrate was strongly cooled, and then crystals separated out. The crystals were scooped out and were recrystallized from ether. (Yield: crude 1.06 g. Found: N, 12.08. Calculated for $C_{11}H_{24}N_2O_3$: N, 12.07%.)

(13) **Dimethylolurea-*n*-amylether** $C_{13}H_{28}N_2O_3$. *n*-Amyl alcohol (5 g.) and one drop of 5 N hydrochloric acid were added to 1 g. of dimethylolurea and were dissolved. After allowing the solution to stand for 20 minutes, it was neutralized with silver carbonate, and was filtered. The filtrate was evaporated and dried. The dried substance was heated and extracted with ether. When the extract was cooled, crystals separated out. The crystals were scooped out and were recrystallized from ether. (Yield: crude 1.0 g. Found: N, 10.80. Calculated for $C_{13}H_{28}N_2O_3$: N, 10.76%.)

(14) **Dimethylolureadibenzylether** $C_{17}H_{20}N_2O_3$. Dimethylolurea (1 g.) was dissolved by adding 5 g. of benzyl alcohol and one drop of 5 N hydrochloric acid. After the solution was allowed to stand for 5 minutes, it was neutralized with silver carbonate and was filtered. When the filtrate was strongly cooled, crystals separated out. The crystals were scooped out and were dissolved in benzene. On adding ether to this solution, crystals separated out. (Yield: 1.0 g. Found: N, 9.24, Calculated for $C_{17}H_{20}N_2O_3$: N, 9.33%.)

(15) **Dimethylolureadiethylthioether** $C_7H_{16}N_2S_2O$. When 5 g. of dimethylolurea was added to 13 g. of ethylmercaptane, to which 10 drops of 5 N hydrochloric acid had been added beforehand, a soft lump was produced. After washing it thoroughly with water, it was heated with alcohol and dissolved. When the solution was cooled, crystals separated out. The crystals were scooped out and were recrystallized from alcohol. (Yield: 5.5 g. Found: C, 41.84: H, 7.78; N, 13.25; S, 30.76. Calculated for $C_7H_{16}N_2S_2O$: C, 40.33; H, 7.74; N, 13.45; S, 30.78%.)

(16) **Methylenebismethylolureadimethylether** $C_7H_{16}N_4O_4$. Methyl alcohol (100 c.c.) and 0.5 c.c. of 5 N hydrochloric acid were added to 3.77 g. of methylenebismethylolurea, and after allowing it to stand for 10 minutes, it was neutralized with silver carbonate, and was heated at 60°C., and was filtered. When the filtrate was cooled, crystals separated out. The crystals were scooped out and were recrystallized from methyl alcohol. (Yield: 2.71 g. Found: C, 37.88; H, 7.34; N, 25.76%; mol. wt., 223.9; CH_2O, 41.13%. Calculated for $C_7H_{16}N_4O_4$: C, 38.15; H, 7.33; N, 25.45; mol. wt., 220.2. Calculated for $3CH_2O/C_7H_{16}N_4O_4$: CH_2O, 40.90%.)

(17) **Dimethyloltrimethylenetetraureadimethylether** $C_{11}H_{24}N_8O_6$. Urea (95 g.) was dissolved in 1000 c.c. of 38% formalin, and the solution was filtered. Then the filtrate was cooled to −6.5°C., and when 10 c.c. of conc. hydrochloric acid was added, in 10 minutes, it yielded white turbidity. Leaving it to stand for one hour the precipitate was scooped out and was washed with alcohol. (Yield: 39.4 g. Found: C, 36.09; H, 6.63; N, 30.68; CH_2O, 43.45. Calculated for $C_{11}H_{24}N_8O_6$: C, 36.25; H, 6.60; N, 30.75. Calculated for $5CH_2O/C_{11}H_{24}N_8O_6$: CH_2O, 41.20%.)

(18) **Monomethylolurea peroxide** $C_2H_6N_2O_3$. Monomethylolurea (2.2 g.) was dissolved in 66 c.c. of 3% hydrogen peroxide (slightly acidic to litmus). The solution was dried by evaporation. This dried substance was dissolved in a small quantity of water by heating. When this solution was cooled, crystals separated out. The crystals were scooped out and were recrystallized from 50% alcohol. (Yield: 1.92 g. Found: C, 22.33; N, 26.63%; mol. wt., 98.8; avail. O, 15.30%. Calculated for $C_2H_6N_2O_3$: C, 22.64; N, 26.42%; mol. wt., 106.0. Calculated for $O/C_2H_6N_2O_3$: avail. O, 15.09%.)

(19) **Hexamethyloltriurea peroxide** $C_9H_{29}N_6O_{11}$, **Crystalline peroxide** $(C_3H_6N_2O_3)_n$ **and Liquid peroxide.** (A) *Hexamethyloltriurea peroxide.* Dimethylolurea (20 g.) was dissolved

in 500 c.c. of 3% hydrogen peroxide (slightly acidic to litmus), and when the solution was evaporated, there remained liquid. This was washed with carbon tetrachloride and ether, and then was dissolved in alcohol. Next, when a portion of insoluble substance was removed, and the solution was evaporated, solid remained. This solid was again dissolved in alcohol, ether was added to the solution, and precipitate separated out. (Yield: crude 5 g. Found: N, 21.30%; mol. wt., 383.2. Calculated for $C_9H_{20}N_6O_{11}$: N, 21.60%; mol. wt., 388.2.)

(B) *Crystalline peroxide.* When 2.5 g. of dimethylolurea was dissolved in 50 c.c. of 3% hydrogen peroxide, and 0.5 c.c. of 5 N hydrochloric acid was added to it, crystals separated out. (Yield: 2.06 g. Found: C, 30.48; H, 5.29; N, 23.65; avail. O, 13.73. Calculated for $C_3H_6N_2O_3$: C, 30.49; H, 5.12; N, 23.73. Calculated for $O/C_3H_6N_2O_3$: avail. O, 13.55%.)

(C) *Liquid peroxide.* Dimethylolurea (12 g.) was dissolved in 500 c.c. of 3% hydrogen peroxide which had been neutralized with barium hydroxide, and when the solution was evaporated, there remained liquid. This liquid was dissolved in alcohol, and a small quantity of the insoluble substance was removed, and the solution was evaporated, and liquid was obtained. When this liquid was poured into ether, it became slightly turbid. The turbidity was filtered, and then the filtrate was evaporated, there remained liquid.

(20) **N,N′-Dimethylolurondimethylether** $C_7H_{14}N_2O_4$. Barium hydroxide (5 g.) and 60 g. of urea were dissolved in 320 c.c. of 38% formalin, and when the solution was heated in boiling water for 10 minutes, and was evaporated, there remained slightly sticky liquid. This was dissolved in the mixture of 1 l. of methyl alcohol and 6 c.c. of conc. hydrochloric acid, and after leaving the solution to stand for 15 minutes, it was neutralized with barium hydroxide, and was filtered. A slightly fluid liquid remained when the filtrate was evaporated. After the inorganic salt was removed by treating it with chloroform, and dimethylolureadimethylether also was removed by treating it with ether, it was subjected to vacuum distillation for refining. (Yield: crude 126 g. Found: C, 43.86; H, 7.73; N, 14.74%; mol. wt., 188.5; CH_2O, 59.32%. Calculated for $C_7H_{14}N_2O_4$: C, 44.19; H, 7.42; N, 14.72%; mol. wt., 190.1. Calculated for $4CH_2O/C_7H_{14}N_2O_4$: CH_2O, 63.16%.)

(21) **N,N′-Dimethylolurondiethylthioether** $C_9H_{18}N_2S_2O_2$. *N,N′*-Dimethylolurondimethylether (10 g.) was dissolved in 14 g. of ethylmercaptane, and when 3 drops of conc. hydrochloric acid were added thereto, heat generated, and the temperature of the solution rose. After cooling, it was neutralized with barium hydroxide, and inorganic salt was removed by the treatment with ether, and when it was evaporated, there remained transparent liquid. When this liquid was subjected to vacuum distillation, the greater part distilled at 125–134°C. (0.1 mm.), and when left to stand, it crystallized. The crystals were dissolved in a small quantity of alcohol, and crystals were separated out by adding water to the solution. (Yield: crude 14.8 g. Found: C, 43.19; H, 7.37; N, 11,16; S, 25.33%; mol. wt., 240 6. Calculated for $C_9H_{18}N_2S_2O_2$: C, 43.15; H, 7.25; N, 11.19; S, 25.62%; mol. wt., 250.3.)

(22) **N-Methyl-N′-methyloluronmethylether** $C_6H_{12}N_2O_3$. Barium hydroxide (3 g.) and 10 g. of methylurea were dissolved in 42.7 c.c. of 38% formalin, and after the solution was heated in boiling water for 10 minutes, it was evaporated. Then, a slightly sticky liquid remained. This was dissolved in the mixture of 100 c.c. of methyl alcohol and 2.5 c.c. of conc. hydrochloric acid. After leaving it to stand for 15 minutes, it was

neutralized with barium hydroxide, and was filtered. When the filtrate was evaporated, there remained slightly fluid liquid. This was treated with chloroform in order to remove inorganic salt, and then, was subjected to vacuum distillation for refinement. (Yield: crude 15.0 g. Found: C, 44.28; H, 7.93; N, 17.43%; mol. wt., 162.5; CH_2O, 53.27%. Calculated for $C_6H_{12}N_2O_3$: C, 44.97; H, 7.56; N, 17.50%; mol. wt., 160.1. Calculated for $3CH_2O/C_6H_{12}N_2O_3$: CH_2O, 56.25%.)

(23) **N-Methyl-N′-methyloluronethylthioether** $C_7H_{14}N_2SO_2$. *N*-Methyl-*N′*-methylol-uronmethylether (6.2 g.) was dissolved in 12.4 g. of ethylmercaptane, and when 3 drops of conc. hydrochloric acid were added thereto, the temperature of the solution rose, heat being generated. After cooling, it was neutralized with barium hydroxide, and again was treated with ether to remove inorganic salt. On evaporation, a transparent liquid remained. This liquid was washed with water, and was refined through vacuum distillation. (Yield: crude 5.8 g. Found: C, 43.91; H, 7.65; N, 14.52%; mol. wt., 186.4. Calculated for $C_7H_{14}N_2SO_2$: C, 44.16; H, 7.42; N, 14.73%; mol. wt., 190.2.)

(24) **N-Ethyl-N′-methyloluronmethylether** $C_7H_{14}N_2O_3$. Barium hydroxide (4 g.) and 22.5 g. of ethylurea were dissolved in 81 c.c. of 38% formalin, and the solution was heated in boiling water for 10 minutes. After evaporation, there remained a slightly sticky liquid. This liquid was dissolved in the mixture of 200 c.c. of methyl alcohol and 5 c.c. of conc. hydrochloric acid. After leaving it to stand for 15 minutes, it was neutralized with barium hydroxide, and was filtered. The filtrate was evaporated, and then slightly fluid liquid remained. This liquid was treated with chloroform in order to remove inorganic salt contained in it. Then, it was refined by vacuum distillation. (Yield: crude 41 g. Found: C, 47.72; H, 8.44; N, 16.23%; mol. wt., 174.1; CH_2O, 46.77%. Calculated for $C_7H_{14}N_2O_3$: C, 48.24; H, 8.10; N, 16.09%; mol. wt., 174.1. Calculated for $3CH_2O/C_7H_{14}N_2O_3$: CH_2O, 51.72%.)

(25) **N-Ethyl-N′-methyloluronethylthioether** $C_8H_{16}N_2SO_2$. *N*-Ethyl-*N′*-methyloluron-methylether (6.6 g.) was dissolved in 12.4 g. of ethylmercaptane. On adding 3 drops of conc. hydrochloric acid to the solution, it generated heat, and its temperature rose. After it was left to cool, it was neutralized with barium hydroxide and was again treated with ether to remove the inorganic salt contained therein. There remained slightly fluid liquid when it was evaporated. Washing it with water, it was subjected to vacuum distillation. It distilled mostly at 110–113°C. (1.0 mm.) and when the distillate was cooled strongly, crystals separated out. (Yield: crude 7.7 g. Found: C, 46.82; H, 8.32; N, 13.62%; mol. wt., 204.6. Calculated for $C_8H_{16}N_2SO_2$: C, 47.01; H, 7.90; N, 13.72%; mol. wt., 204.2.)

(26) **N,N′-Dimethyluron** $C_5H_{10}N_2O_2$ **and Tetramethyldimethylenediureid** $C_8H_{16}N_4O_2$. Barium hydroxide (1.5 g.) and 8.8 g. of *N,N′*-dimethylurea were dissolved in 24 c.c. of 38% formalin, and after heating the solution in boiling water for 5 minutes, it was evaporated. Then, a slightly sticky liquid remained. This liquid was dissolved in the mixture of 150 c.c. of methyl alcohol and 1.5 c.c. of conc. hydrochloric acid. Leaving it to stand for 15 minutes, it was neutralized with barium hydroxide, and was filtered. Through evaporation of the filtrate, there remained a slightly fluid liquid. Removing the inorganic salt contained therein by treatment with chloroform, it was subjected to vacuum distillation. Then, the greater part distilled, leaving crystals. The crystals were recrystallized from alcohol. (Yield: 1.3 g. Found: C, 47.78; H, 8.43; N, 28.00%;

mol. wt., 190.4; CH_2O, 30.07%. Calculated for $C_8H_{16}N_4O_2$: C, 47.95; H, 8.08; N, 27.99%; mol. wt., 200.2. Calculated for $2CH_2O/C_8H_{16}N_4O_2$: CH_2O, 29.99%.)

The distillate was refined by the treatment with the mixture of ethylmercaptane and hydrochloric acid, and was subjected to vacuum distillation. The best part distilled at 64°C. (0.1 mm.). When the distillate was strongly cooled, it formed crystals. These were recrystallized from ether. (Yield: crude 3.5 g. Found: C, 46.96; H, 7.83; N, 21.63%; mol. wt., 131.5; CH_2O, 46.21%. Calculated for $C_5H_{10}N_2O_2$: C, 46.12; H, 7.75; N, 21.53; mol. wt., 130.1. Calculated for $2CH_2O/C_5H_{10}N_2O_2$: CH_2O, 46.14%.)

(27) **N,N-Dimethyl-N'-methylolureamethylether** $C_5H_{12}N_2O_2$. Barium hydroxide (4 g.) and 8.8 g. of *N,N*-dimethylurea were dissolved in 24 c.c. of 38% formalin, and when the solution was heated in boiling water for 10 minutes, and was evaporated, a slightly sticky liquid remained. This liquid was dissolved in the mixture of 100 c.c. of methyl alcohol and 2.8 c.c. of conc. hydrochloric acid, and leaving it to stand for 15 minutes it was neutralized with barium hydroxide, and was filtered. When the filtrate was evaporated a transparent liquid remained. Removing the inorganic salt contained in it by treating it with chloroform, it was left to stand at room temperature. Then, crystals separated out. The crystals were scooped out, and were recrystallized from ether. (Yield: 7 g. Found: C, 45.51; H, 9.29; N, 21.32%; mol. wt., 128.7; CH_2O, 22.78%. Calculated for $C_5H_{12}N_2O_2$: C, 45.42; H, 9.16; N, 21.21%; mol. wt., 132.1. Calculated for $CH_2O/C_5H_{12}N_2O_2$: CH_2O, 22.72%.)

(28) **Methylenebismethyloluronmethylether** $C_{11}H_{20}N_4O_6$. Barium hydroxide (1 g.) and 13.2 g. of methylenediurea were dissolved in 50 c.c. of 38% formalin, and when the solution was heated in boiling water for 10 minutes, and was evaporated, colourless, transparent sticky substance remained. This was dissolved in the mixture of 200 c.c. of methyl alcohol and 1 c.c. of conc. hydrochloric acid. Leaving it to stand for 15 minutes, it was neutralized with barium hydroxide and was evaporated. Then, sticky liquid remained. Removing inorganic salt contained therein by the treatment of chloroform, it was refined with ether. (Yield: crude 27.0 g. Found: C, 42.67; H, 7.84; N, 18.92%; mol. wt., 273.3; CH_2O, 63.73%. Calculated for $C_{11}H_{20}N_4O_6$: C, 43.39; H, 6.63; N, 18.42%; mol. wt., 304.2. Calculated for $7CH_2O/C_{11}H_{20}N_4O_6$: CH_2O, 69.03%.)

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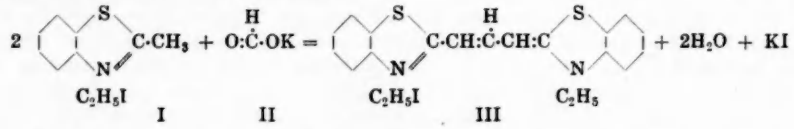
ÜBER CYANINFARBSTOFFE. VIII. EINE NEUE SYNTHESE VON 8-METHYL-TRIMETHINTHIOCYANIN-DERIVATEN UND ÜBER DIE REAKTIONSFÄHIGKEIT DER 8-METHYLGRUPPE.

Von Terutaro OGATA.

Eingegangen am 14. November 1935. Ausgegeben am 28. März 1936.

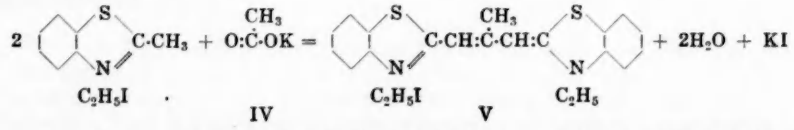
Zur Darstellung der für die Photographie wertvollen 8-Methylthiocyanin-Derivate, beim mittelständigen C-Atom der Trimethinkette durch CH_3-substituiert, sind in letzter Zeit 2 Verfahren ausgearbeitet worden. Hamer[1] hat durch Einwirkung des Orthoessigsäureäthylesters auf einer Lösung von μ-Methylbenzothiazoläthyljodid (I) in Pyridin oder Essigsäureanhydrid 8-Methylfarbstoffe erhalten. Kürzlich haben dann Brooker und White[2] nach interessanten Versuchen die quartären Salze der μ-Methylbenzothiazol-Derivate durch Erhitzen mit Pyridin bei Gegenwart von Triäthylamin in 8-Methylfarbstoffe überzuführen vermocht.

Vor einigen Jahren habe ich aus Jodäthylat (I) durch Einwirkung von K-formiat (II) in Gegenwart von Essigsäureanhydrid 20% iger Ausbeute Trimethinthiocyanin (III) erhalten.



I II III

Bald danach habe ich durch Anwendung von K-acetat (IV) statt des K-formiats, als Quelle des zentralen Äthenylradikals des Farbstoffmoleküls, einen kupferroten Farbstoff gewonnen (man konnte hierbei Bildung von 8-Methylthiocyanin (V) erwarten). Die Reaktion kann in folgender Gleichung ausgedrückt werden:

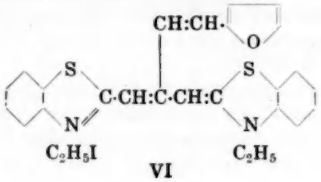


IV V

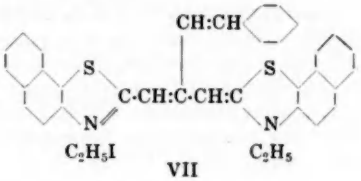
Der oben erwähnte 8-Methylfarbstoff (V) hat mit dem Trimethinthiocyanin (III) charakteristische Eigenschaften gemeinsam, nur ist er wesentlich wirksamer, vor allem gegen Aldehyd, mit dem er kondensiert wird. Unter

(1) F. M. Hamer, *J. Chem. Soc.*, **1928**, 160.
(2) L. G. S. Brooker und F. L. White, *J. Am. Chem. Soc.*, **57** (1935), 547.

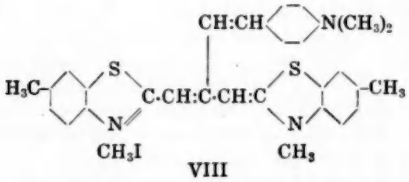
Einwirkung eines Aldehyds (z.B. des Furfurols) auf dem 8-Methylfarbstoff in Gegenwart von Piperidin entstand ein Furfur-vinylfarbstoff (VI), der analytisch bestimmt wurde.



VI



VII



VIII

Versuche, aus dem 1,1′,4,4′,8-Pentamethyl-trimethinthiocyanin (3)[3] und dem 1,1′-Diäthyl-8-methyl-dibenzo-trimethinthiocyanin (4)[3] mittels eines Aldehyds (z.B. des Benzaldehyds oder des *p*-Dimethylaminobenzaldehyds) Vinylfarbstoffe (z.B. VII, VIII) darzustellen, waren auch erfolgreich. Die neuen Vinylfarbstoffe sind gut wirkende Sensibilisatoren für photographische Emulsionen (nach der Orientalischen Photographischen Industriellen Akt.-Ges., Tokio). Spektroskopisch ist eine erhebliche Verschiebung des Absorptionsbandes nach dem Gebiet der längeren Wellen hin bemerkenswert.

Beschreibung der Versuche.

Trimethinthiocyanin aus μ-Methylbenzothiazoläthyljodid und K-formiat. (1) 1,1′-Diäthyl-trimethinthiocyaninjodid (III) wird aus 0.6 g. μ-Methyl-benzothiazoläthyljodid (I) und 0.6 g. K-formiat (II) in Gegenwart von 1 c.c. Essigsäureanhydrid durch 30 Minuten langes Erhitzen bei 150° dargestellt. Das Rohprodukt wurde mit Äther und dann mit Wasser gewaschen. Aus Methylalkohol kristallisiert es in hellblauen Säulen vom Schmp. 269° (unter Zersetzung), der mit einem nach der Dianil-Methode[4] gewonnenen Präparat durch den Misch-schmp. festgestellt wurde. Abs.-max. 560 mμ, Sens.-max. 590 mμ. (Gef.: I, 26.11; S, 12.53. Ber. für $C_{21}H_{21}N_2IS_2$: I, 25.78; S, 13.03%.)

8-Methylfarbstoffe aus Alkyljodiden und K-acetat. (2) 1,1′-Diäthyl-8-methyl-trimethinthiocyaninjodid (V). Ein Gemisch von 0.6 g. (2 Mol) μ-Methylbenzothiazoläthyljodid (I), 0.1 g. (1 Mol) K-acetat und 0.4 c.c. Essigsäureanhydrid wurde 60 Minuten lang bei 165° erhitzt. Durch Waschen zuerst mit Äther, dann mit Wasser und Alkohol konnte der Farbstoff fast rein erhalten werden. Das Rohprodukt (0.21 g.) wird aus 60 c.c. Methylalkohol umkristallisiert und er gibt kupferrote Kristalle (doch manchmal stahlblaue

(3) Siehe die Beschreibung der Versuche.
(4) T. Ogata, *Proc. Imp. Acad. Japan*, **9** (1933), 604.

Nadeln), die bei 286° schmelzen (Zers.); Ausbeute 0.15 g. (30%). Abs.-max. 540 mμ, Sens.-max. 580 mμ. (Gef.: I, 25.45; S, 12.50. Ber. für $C_{22}H_2N_2IS_2$: I, 25.07; S, 12.67%.)

(3) 1,1′,4,4′,8-Pentamethyl-trimethinthiocyaninjodid bildete sich durch halbstündiges Erhitzen (bei 165°) einer Lösung von 0.3 g. 2,5-Dimethylbenzothiazolmethyljodid und 0.05 g. K-acetat in 0.2 c.c. Essigsäureanhydrid. Stahlblaue Kristalle aus Methylalkohol. Schmp. 279° (Zers.); Ausbeute 20%. Abs.-max. 540 mμ, Sens.-max. 580 mμ. (Gef.: I, 25.09; S, 12.27. Ber. für $C_{22}H_{23}N_2IS_2$: I, 25.07; S, 12.67%.)

(4) 1,1′-Diäthyl-8-methyl-3,4,3′,4′-dibenzo-trimethinthiocyaninjodid wird aus α-Methyl-β-naphtothiazoläthyljodid und K-acetat wie Farbstoff (2) hergestellt. Grün glänzende Nädelchen aus Methylalkohol. Schmp. 293° (Zers.); Ausbeute 7%. Abs.-max. 590 mμ, Sens.-max. 600 mμ. (Gef.: I, 20.65; S, 10.34. Ber. für $C_{30}H_{27}N_2IS_2$; I, 20.93; S, 10.58%.)

Einwirkung von Aldehyden auf 8-Methylfarbstoffe. (5) 1,1′-Diäthyl-8-furfur-vinyl-trimethinthiocyaninjodid (VI) wird aus 0.25 g. 8-Methyl-trimethincyanin (2), 0.5 c.c. Furfurol und 2 c.c. Alkohol in Gegenwart von 15 Tropfen Piperidin durch etwa 30 Minuten langes Erhitzen bei 90° dargestellt. Die rote Farbe der Lösung schlägt dann in violett um. Das Rohprodukt wird nach dem Erkalten abgesaugt. Schöne, grün glänzende Kristalle aus Methylalkohol. Schmp. 277° (Zers.); Ausbeute 0.09 g. Abs.-max. 560 mμ. (Gef: I, 22.85. Ber. für $C_{27}H_{25}ON_2IS_2$: I, 22.99%.)

(6) 1,1′-Diäthyl-8-phenyl-vinyl-trimethinthiocyaninjodid. 0.25 g. 8-Methyltrimethinthiocyanin (2) wurde mit 0.1 c.c. Benzaldehyd in 1 c.c. Alkohol und 5 Tropfen Piperidin 15 Minuten lang bei 90° erwärmt. Nach dem Waschen mit Alkohol wurde der Rückstand aus Methylalkohol umkristallisiert. Stahlblaue Kristalle vom Schmp. 266° (Zers.); Ausbeute 0.17 g. Abs.-max. 560 mμ, Sens.-max. 600 mμ. (Gef.: I, 21.26; S, 10.76. Ber. für $C_{29}H_{27}N_2IS_2$: I, 21.36; S, 10.80%.)

(7) 1,1′-Diäthyl-8-phenyl-vinyl 3,4,3′,4′-dibenzo-trimethinthiocyaninjodid (VII) wurde aus 0.18 g. 8-Methylfarbstoff (4) durch 3/4 stündiges Erhitzen bei 90° mit 0.06 c.c. Benzaldehyd in 1 c.c. Alkohol und 8 Tropfen Piperidin gewonnen. Grün glänzende Kristalle aus Methylalkohol. Schmp. 265° (Zers.); Ausbeute 0.12 g. Abs.-max. 610 mμ. (Gef.: I, 18.58; S, 8.91. Ber. für $C_{37}H_{31}N_2IS_2$: I, 18.28; S, 9.24%.)

(8) 1,1′-Diäthyl-8-*p*-dimethylaminophenyl-vinyl-trimethinthiocyaninjodid. 0.5 g. 8-Methyl-trimethinthiocyanin (2) wurde mit 0.2 g. *p*-Dimethylaminobenzaldehyd in 3 c.c. Alkohol und 15 Tropfen Piperidin 25 Minuten lang bei 90° erhitzt. Grüne glänzende Kristalle. Schmp. 252° (Zers.); Ausbeute 0.22 g. Abs.-max. 560 mμ, Sens.-max. 600 mμ. (Gef.: I, 20.05; S, 9.76. Ber. für $C_{31}H_{29}N_3IS_2$: I, 19.92; S, 10.07%.)

(9) 1,1′,4,4′-Tetramethyl-8-*p*-dimethylaminophenyl-vinyl-trimethinthiocyaninjodid(VIII) wurde aus 0.2 g. 8-Methylfarbstoff (3) und 0.08 g. *p*-Dimethylaminobenzaldehyd wie Farbstoff (8) dargestellt. Man reinigte es durch Umkristallisation aus Methylalkohol (750 c.c. per 1 g.). Grüne Kristalle vom Schmp. 292° (Zers.); Ausbeute 0.07 g. Abs.-max. 570 mμ. (Gef.: I, 20.23; S, 9.75. Ber. für $C_{31}H_{32}N_3IS_2$: I, 19.92; S, 10.07%.)

(10) 1,1′-Diäthyl-8-*p*-dimethylaminophenyl-vinyl-3,4,3′,4′-dibenzotrimethinthiocyaninjodid entsteht aus 0.3 g. Farbstoff (4) und 0.1 g. *p*-Dimethylaminobenzaldehyd auf ähnliche Weise wie Farbstoff (9). Grüne, metallisch glänzende Kristalle. Schmp. 288°; Ausbeute 0.1 g. Abs.-max. 610 mμ. (Gef.: I, 17.17; S, 8.74. Ber. für $C_{39}H_{36}N_3IS_2$: I, 17.22; S, 8.60%.)

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THE CONSTITUTION OF AWOBANIN AND AWOBANOL, THE COLOURING MATTER OF AWOBANA[1] AND ITS CO-PIGMENT.

By Miss Chika KURODA.

Received November 16th, 1935. Published March 28th, 1936.

Flowers of "Tsuyukusa", *Commelina communis*, are beautiful azure blue and the extracted flower juice colours fabrics blue, hence the name "Tsukikusa" or "Awobana", meaning a paint grass or a blue flower. The colouring matter is one of the most well known and the oldest of its kind in Japan and the usage has a historical interest. Though no longer in practical use as a dye, as the colour can be easily washed away, it is still employed for drawing patterns in the art of "Yuzen" silk print and "Shiborizome" (tied dyeing). In some regions, therefore, the plant is especially cultivated for the production of "Awobana paper" which is painstakingly prepared by painting the flower juice on sheets of paper and drying them in the sun. No record of the chemical study on this pigment has been found.

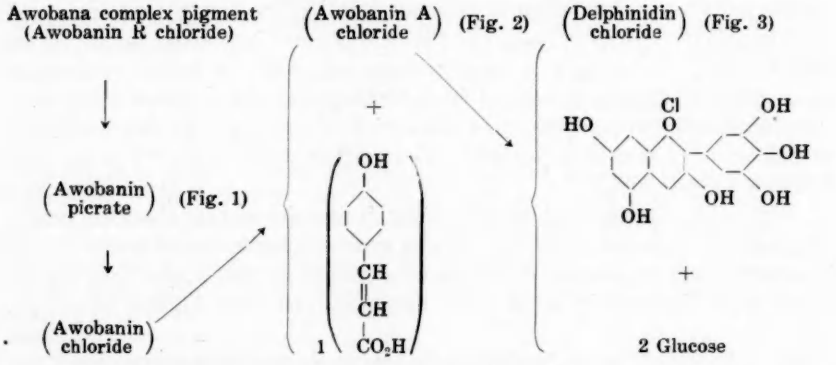
The present author was attracted to the study of this pigment, which she desired first, to obtain in a pure crystalline state, though it was difficult. However, beautiful blue coloured precipitate, like ultramarine, was finally isolated on adding methyl alcohol to its aqueous solution prepared from the Awobana paper. The blue powder thus obtained remarkably kept the colour unchanged in dry state (even in aqueous solution the colour was preserved considerably). In this respect the pigment seemed unusually stable for an anthocyanin; furthermore by decomposition with alkali, *p*-hydroxy-acetophenone which is not usually derived from anthocyanin was produced along with *p*-coumaric acid. Therefore, the constitution of this pigment was considered to belong to a special series and not to anthocyanin, and the study was followed accordingly.

However, after several investigations, it was shown that the main bright colour of this pigment is due to an anthocyanin awobanin named by the author in presence of a co-pigment awobanol also named by the author and metals which were detected in ashes after combustion (K, Mg, Al, SO_4, PO_4, etc.).

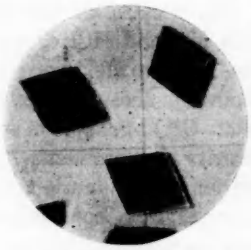
(1) "Awobana" is the local name for the flower of *Commelina communis var. hortensis* Makino used in Shiga, where the commercial Awobana paper is produced. It may not be synonymous with the so-called "Awobana" or "Tsuyukusa" (*Commelina communis*).

The above results were already reported in short notes.[2] Now, to summarise details of the above study and to report some new results, the present communication is made.

Notwithstanding difficulties in the separation of awobanin from awobanol because of their properties which resemble each other in many respects, the two were finally separated and the constitution of awobanin was successfully confirmed as follows. Awobana paper was steeped in water, to the solution, an aqueous lead acetate solution was added to precipitate the lead salt of the pigment. On treating the lead salt with CH_3OH–HCl, it was converted into the chloride (red) in methyl alcoholic solution. The chloride of the colouring matter was precipitated by the addition of ether several times, then a red powdery pigment was obtained as chloride. The isolation of pure anthocyanin from the above chloride was exceedingly difficult, however, after careful treatments, a new crystalline glucoside of the pigment awobanin was obtained as picrate (Fig. 1), and finally as chloride. Awobanin was confirmed to be a compound of another authocyanin (delphinidin 3,5-diglucoside, awobanin A named by the author) and *p*-coumaric acid by the following procedures. Analytical results of the picrate and the chloride agreed with delphinidin picrate+2 glucose+*p*-coumaric acid+$5H_2O$ and delphinidin chloride+2 glucose+*p*-coumaric acid+$5H_2O$, respectively. When awobanin was treated with cold alkali in H_2 gas, *p*-coumaric acid as one of the above component was isolated quantitatively. As another component, crystalline glucoside awobanin A finally separated slowly, when awobanin was specially treated with 20% aqueous HCl at room temperature and left for several days. The identification of awobanin A thus obtained is shown below.

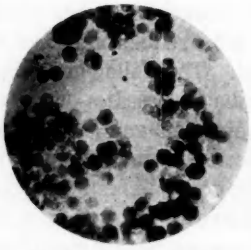


(2) Kuroda, *Proc. Imp. Acad. Japan*, **7** (1931), 61. Kuroda, *ibid.*, **9** (1933), 94. Kuroda, *ibid.*, **11** (1935), 238.



Awobanin picrate

Fig. 1.



Awobanin A chloride

Fig. 2.

Awobanin aglucone

Fig. 3.

Upon recrystallization, needle crystals were obtained from methyl alcohol and prisms from CH_3OH–HCl (Fig. 2). On analysis, both forms were found to agree with diglucoside of delphinidin chloride $C_{27}H_{31}O_{17}Cl+3H_2O$. The estimation of sugar was carried out by Pavy's method, the result being in agreement. When hydrolyzed with HCl, 1 mol of aglucone and 2 mols of sugar were produced. From the sugar, glucosazone was formed, agreeing in the properties and the melting point. The aglucone (Fig. 3) crystallized out in prisms from CH_3OH–HCl, and it gave all the reactions of delphinidin.

The analysis showed the compound to be delphinin chloride $C_{15}H_{11}O_7Cl+3H_2O$. Alkali fusion was applied to the aglucone and the glucoside. Phloroglucinol which was confirmed by the reactions and the analytical results, and also an acid which was precipitated with lead acetate were formed. The latter seems to be gallic acid by qualitative tests, etc., and was converted into trimethyl ether with dimethyl sulphate, which melted at 168° (gallic acid trimethyl ether melts at 168°). Micro-Zeisel estimation proved the absence of methoxyl groups in the aglucone.

Now the position of the glucose was confirmed to be "3" and "5" by Karrer's perhydrol method.[3] Furthermore colour reactions with Na_2CO_3 and with buffered solution were exactly in agreement with "delphinin chloride", 3,5-diglucoside of delphinidin chloride in literature.[4] Absorption spectrum was observed to be similar to the diglucoside of delphinidin chloride. The yield of the diglucoside was considerable. Delphinidin monoglucoside was also noticed.

A crystalline co-pigment awobanol was obtained from the blue aqueous solution prepared from the Awobana powder, or Awobana paper, when it was heated with HCl. This compound seemed to be closely related to the chief

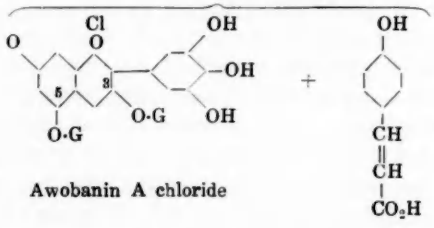
(3) *Helv. Chim. Acta*, **15** (1932), 1212.

(4) Reynols, Robinson, and Scott-Moncrieff, *J. Chem. Soc.*, **1934**, 1235.

pigment because of the comparatively large yield, and because of the red colouration which was shown on reduction either with Mg and HCl or with sodium amalgam in alcohol. The following studies were made upon this substance: analyses of awobanol (needles or plates) and its acetyl derivative (crystalline); acetyl determination and estimation of CH_3O-group. Alkali fusion gave *p*-hydroxy-benzoic acid and a small quantity of a product which shows the phloroglucinol reaction. Alkali decomposition also gave the above phenol, however, *p*-hydroxy-acetophenone was produced in a considerable quantity. Consequently it was assumed that awobanol is not directly related to the chief Awobana pigment and rather a co-pigment.

In concluding, the pigment in Awobana is considered to be the anthocyanin combined with *p*-coumaric acid and co-pigment awobanol.

Awobanin chloride



Awobanin A chloride

G = Glucose

The further study of the positions of *p*-coumaric acid, the co-pigment and the relations of the ashes with Awobana pigment is in progress.

Experimental.

Isolation of Awobanin. The commercial Awobana paper (800 g.) was extracted with cold water, to the resulting blue coloured solution, an aqueous lead acetate solution was added to precipitate the lead compound of the pigment; the precipitate was sucked, and dried on a tile (blue powder 100 g.). On treating the lead salt with CH_3OH–HCl (2%) it was converted into chloride in CH_3OH solution. From the resulting red solution chloride of pigment was precipitated by the addition of ether (yield 25 g.). The chloride was dissolved in absolute CH_3OH, from which the pigment was precipitated as a red powdery substance on addition of ether. Though the process was repeated several times, the pigment seemed to contain some quantity of awobanol and other impurity. Furthermore as the chloride was very easily soluble in water or CH_3OH, the isolation of the crystalline pigment from the substance was extremely difficult. The chloride was named awobanin chloride (R) by the author.

However it was finally successfully obtained in crystalline state after several experiments and especially by using the material prepared from fresh flowers, instead of Awobana paper. However, as it was generally difficult to have the material of the

Awobana pigment directly, from the fresh flowers, the author has usually studied with the material which was prepared from Awobana paper, except the above one occasion.

The fresh flowers were extracted with CH_3OH–HCl (2%) in cold; from the resulting red solution the lead salt of pigment was precipitated, and was converted into its chloride, and was purified in the usual way as mentioned above. To the solution of the chloride (R) thus obtained (7 g.) dissolved in hot H_2O (30 c.c.), picric acid (3 g.) was added, heated on the water bath, and left for one day, then an oily matter separated. When the oily matter was carefully treated with dilute aqueous picric acid on the water bath, picrate of the pigment crystallized out in reddish brown lustrous plates (2 g.). (Found for air dried material: C, 46.00, 46.06; H, 4.64, 4.68; N, 3.84, 3.93. Calculated for $C_{42}H_{39}O_{26}N_3+5H_2O$: C, 46.19; H, 4.49; N, 3.85%.) This was recrystallized from picric acid+CH_3OH (Fig. 1). The picrate was converted into chloride, when ether was added to the picrate dissolved in 2% CH_3OH–HCl, then the chloride crystallized out in red fine needles (decomposition over 200°). (Found for air dried material: C, 48.31, H, 5.54; Cl, 3.60. Calculated for $C_{26}H_{37}O_{19}Cl+5H_2O$: C, 48.1; H, 5.23; Cl, 3.8%.) This substance was easily soluble in cold water or methyl alcohol, giving a purple red colour. With sodium carbonate it gave a pure blue colour fading to clear green.

Decomposition of Awobanin with Cold Alkali. Awobanin (0.1 g.) dissolved in water (2.5 c.c.) was treated with cold aqueous NaOH (5 c.c.) in H_2 for 2 hours. The product was acidified, extracted with ether. *p*-Coumaric acid (white crystals, m. p. 208° both alone and after admixture with an authentic specimen) was isolated from the ethereal solution. (Found for material dried on H_2SO_4; C, 65.8; H, 5.0. Calculated for $C_9H_8O_3$ C, 65.9; H, 4.9%.)

When awobanin R was decomposed with hot aqueous alkali in H_2 gas, *p*-coumaric acid and *p*-hydroxy-acetophenone were isolated.

Isolation of Awobanin A. The solution of awobanin chloride (R) (1 g.) dissolved in cold 20% aqueous HCl was left for few days at room temperature; dark purple substance gradually crystallized out (0.5 g.), it was washed with CH_3OH, then with 0.5% aqueous HCl (yield 0.25 g.). For analysis a specimen was recrystallized from CH_3OH (air dry). (Found: C, 45.43: H, 5.11; Cl, 4.77. Calculated for $C_{27}H_{31}O_{17}Cl+3H_2O$: C, 45.25; H, 5.17; Cl, 4.60%.) This substance was purified under several conditions as follows: (1) From CH_3OH–HCl (2%) it crystallized in needles; (2) When it was dissolved in minimum quantity of 0.5% hot aqueous HCl and an equal volume of 3% C_2H_5OH–HCl was added, it crystallized out in plates (Fig. 2). However, analytical results were identical.

Direct Comparison of Colour Reactions of Awobanin A and Nasunin A Chloride. Both specimens were recrystallized in the same way with different results as follows. The compound was dissolved in a minimum quantity of 0.5% hot aqueous HCl and an equal volume of 3% C_2H_5OH–HCl was added. After cooling, awobanin A chloride crystallized out in small hexagonal plates with golden lustre while the other separated in fine needles with golden lustre.

The colour reactions in buffered solution of the above two specimens recrystallized in the same way were compared. The colours given by the two pigments were almost identical except that awobanin A became red at a lower *p*H than nasunin A: (1) rose-pink, fading slowly; (2) rose-pink; (3) (4) the same, fading to very pale pink rapidly; (5) (6) bluish-pink, becoming colourless rapidly; (9) (10) blue-violet; (11) violet-red; (13) violet-blue; (14) violet; (15) deep blue.

Both specimens were very sparingly soluble (or insoluble) in cold water, alcohol, and dilute aqueous HCl but readily in hot dilute aqueous HCl. All the ordinary reactions, the colours with Na_2CO_3 (a bright pure blue) and with $FeCl_3$ in alcoholic solution (violet-blue) were observed identical.

Hydrolysis of Awobanin A with Hot Acid. (1) *Isolation of delphinidin chloride (aglucone) from awobanin A.* When awobanin A (0.1 g.) was boiled with 20% aqueous HCl for three minutes, chloride of aglucone separated. This was crystallized under the same conditions with nasunidin chloride. The aglucone crystallized out in plates with a green metallic lustre which was quite identical with delphinidin chloride from nasunin A. (Found: C, 45.75; H, 4.08. Calculated for $C_{15}H_{11}O_7Cl+3H_2O$: C, 45.9; H, 4.33%.)

(2) *The colour reactions with buffered solution.* The both specimens, the aglucones from nasunin and awobanin chlorides gave quite identical results agreeing with those of delphinidin chloride in the literature: (1) red, pink in 30 seconds; (2) violet red, colourless in 30 seconds; (3) permanganate, colourless in 30 second; (4) similar to (3); (5) violet; (6) deep violet red; (9) blue violet; (10) similar to (9); (11) blue violet; (13) blue violet dichromic, pale yellow in $1^1/_2$ hours; (14) indigo blue, pale yellowish gray in $1^1/_2$ hours; (15) (16) similar to (14).

(3) *Estimation of sugar.* The above resulting 20% aqueous HCl solution (the filtrate from the aglucone) was neutralized with alkali and dried. The dry mass was treated under the same conditions with nasunin A and sugar was estimated by Pavy's method. (Found: sugar, 47.81. Calculated for $C_{27}H_{31}O_{17}Cl+3H_2O$: sugar, 50.28%.)

(4) *The position of sugar.* Awobanin A chloride (0.3 g.) was treated with 30% H_2O_2 as in the case of kuromamin (see following paper) and glucosazone was separated from position 3; m.p. 205°, 0.04 g. The filtrate from the above osazone was heated with 15% aqueous HCl on the water bath for $1^1/_2$ hours, then filtered. The filtrate was neutralized with alkali and dried in vacuum. From the residue, glucosazone was isolated by aid of $C_6H_5NH{\cdot}NH_2HCl$ and sodium acetate as usual. After purifying, yield 0.06 g.; m.p. 203° alone and in mixed sample with an authentic specimen. Micro-Zeisel estimation proved the absence of methoxyl groups in the aglucone.

Alkali Fusion of Awobanidin (Aglucone of Awobanin). Awobanidin chloride (0.8g.) was fused with NaOH (0.5 g.) and a small quantity of water at 203°, after cooling, the product was acidified with HCl, extracted with ether; the ether was evaporated, and from the ethereal residue dissolved in water, lead salt was precipitated by addition of lead acetate, the precipitate (yellowish brown) was filtered, (filtrate A). The precipitate was washed with water, then decomposed with dilute H_2SO_4 and extracted with ether; the ethereal residue dissolved in a small quantity of CH_3OH, was methylated with $(CH_3)_2SO_4$ and 50% aqueous KOH in H_2 gas; the reaction product was heated on the water bath to decompose the methyl ester and to evaporate CH_3OH, then was acidified, extracted with ether; the ethereal residue was again extracted with hot benzene. The benzene soluble part was crystallized from hot water, then gallic acid trimethyl ether, m.p. 165°, was isolated. The filtrate A was treated with dilute H_2SO_4, and $PbSO_4$ was removed; when the filtrate was extracted with ether, phloroglucinol was isolated, m.p. 208° both alone and after admixture with the authentic specimen. (Found: C, 44.5; H, 6.2. Calculated for $C_6H_3(OH)_3+2H_2O$: C, 44.45; H, 6.7%.)

Absorption Spectra of Awobanin A and Awobanidin Chloride. The substance in each case was dissolved in CH_3OH (N/10000), and iron arc was used as a light source. The photographs taken will be reproduced in another paper.

Preparation of Awobana Powder. Awobana paper was treated with water; to the resulting blue solution, CH_3OH was added, then a blue powder precipitated; this was sucked, and washed with CH_3OH well; the dry powder thus obtained was easily soluble in water giving a beautiful blue colour.

Isolation of Awobanol. The aqueous solution (or prepared directly from Awobana paper) of Awobana powder was heated with aqueous HCl (nearly 3%) for 1–2 hours, and was left. After a few days a red oily matter gradually separated and solidified. After filtering, the red powder was treated with CH_3OH, several times, then raw awobanol was obtained in pink needles. After purifying with hot CH_3OH it crystallized out in pale needles (m.p. 216°). This substance was soluble in hot CH_3OH, but insoluble in ether, and gave a brownish violet colour with $FeCl_3$. (Found: C, 57.13; H, 4.54%.) When heated with water it was converted into another yellowish flat crystals (m.p. 256°).

Preparation of Acetyl Derivative of Awobanol. (1) With sodium acetate and acetic anhydride at 100°C. a crystalline product in white needles (m.p. 148–150°) was obtained. (Found: C, 55.99; H, 4.53%.) (2) With acetic anhydride and conc. H_2SO_4 at room temperature, a crystalline product in white needles (m.p. 148–156°) was obtained. (Found: C, 55.99; H, 4.53%.)

Decomposition of Awobanol with Alkali. Awobanol was fused with NaOH in the usual way, the product was acidified, extracted with ether, from the neutral part of the ethereal residue, *p*-hydroxy-acetophenone was isolated, white needles from hot water, m.p. 107° both alone and after admixture with the authentic specimen. (Found: C, 70.23; H, 5.9. Calculated for $C_8H_8O_2$: C, 70.59; H, 5,8%.)

The author desires to thank Professor R. Majima for the kindest advice, the Imperial Academy for a grant, and Miss Mizu Wada for her kind help and also Miss Sumi Matsumoto for chlorine determination.

The R. Majima Laboratory,
the Institute of Physical and Chemical Research.

THE CONSTITUTION OF NATURAL COLOURING MATTERS, KUROMAMIN, SHISONIN, AND NASUNIN.

By Chika KURODA and Mizu WADA.

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"Kuromame", "Shiso", and "Nasu" are widely used vegetables in Japan, and as they are specially favoured for their bright colours, the chemical study of their colouring matters is of great importance as well as of much interest. However almost no literature has been found upon the subjects.

The authors were fortunately successful in isolating their main colouring matters in crystalline state, and after several investigations it was very curious to find that all three of these pigments are anthocyanin. Their short sketches have already been made[1], and now the following details will be recorded.

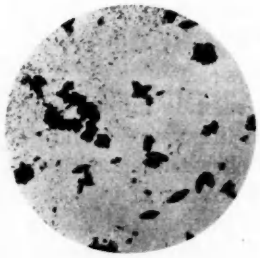
I. Kuromamin, The Colouring Matter of "Kuromame".

"Kuromame"[2] which belongs of *Glycine Soja Benth*, is given the special name because of its delicacy of taste and of the specially deep bluish colour of the seed-coat. Not only used as common food it is specially served as one of happy symbolical sweets in the typical ceremonial menu of New Year. It is also favoured as medicinal matter especially recommended to vocalists. As results of preliminary tests the black pigment was treated as anthocyanin; however, the pigment seemed at first to be a mixture of a water soluble colouring matter and another water insoluble bluish matter. Therefore the treatment was carried out accordingly. From the reddish purple aqueous solution obtained by leaving the beans immersed in cold water, a bluish-green precipitate was formed on addition of aqueous lead acetate. The lead salt was converted into chloride in the usual manner. Isolation of pure pigment from the chloride was exceedingly difficult. However, after several experiments the pigment was successfully obtained by purifying the lead salt with cold acetic acid. The chloride, obtained from the lead salt thus purified, still contained impurities, but the latter dissolved in CH_3OH easily, therefore the isolation of crystalline pigment was finally successful after removing the impurities by special treatment. The glucoside crystallized in green

(1) Kuroda and Wada, *Proc. Imp. Acad. Japan*, **9** (1933), 101; **9** (1933), 517; **11** (1935), 189; **11** (1935), 28; **9** (1933), 51; **11** (1935), 235.

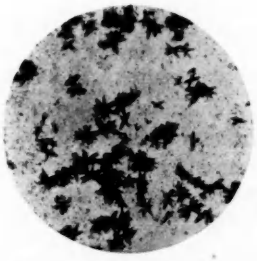
(2) "Kuro" means black and "Mame" bean in Japanese.

leaflets with metallic lustre. Its analytical results and decomposition products with boiling HCl proved to be monoglucoside of cyanidin chloride $C_{21}H_{21}O_{11}Cl + 1^1/_2H_2O$.



Kuromamin chloride from water-soluble pigments from "Kuromame" from Hokkaido

Fig. 1.



Kuromamidin chloride from water-soluble pigments from "Kuromame" from Hokkaido

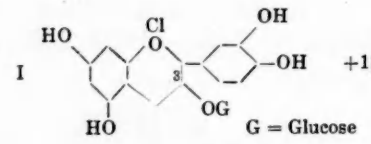
Fig. 2.

The dry seed-coat, after the removal of the above water-soluble colouring matter was treated with CH_3OH–HCl, and the pigment from the resulting red solution, was purified and isolated in crystalline state as chloride by using lead salt method as previously mentioned. The chloride was proved to be monoglucoside of cyanidin chloride $C_{21}H_{21}O_{11}Cl + 1^1/_2H_2O$ by analysis and by its decomposition products as well as by the water-soluble pigment.

By these experiments, the nature of the colouring matter of the seed-coat was shown to be identical whether derived from the water-soluble portion or otherwise. This observation was verified by treating the seed-coat directly with CH_3OH–HCl instead of first treating it with water. The name kuromamin is given to the crystalline glucoside by the authors.

It was suggested that there may exist possible disagreement in the chemical structure of the colouring matter among different samples from unlike localities. Indeed there are amazingly numerous varieties of "Kuromame" on market, differing considerably in their appearances. Such a consideration led to our further studies to apply the above treatment to the beans from Manchuria (Mukden and Shing Tai Tzu). As the results, it was shown that the colouring matters of "Kuromame", regardless of the varieties and the localities, belong to the same kind of compound.

After several investigations, the above glucoside "kuromamin", in every respect, was found to be identical with chrysanthemin (I), namely cyanidin 3-monoglucoside.



Kuromamin (= Chrysanthemin) chloride

The procedures will be pointed out as follows :

(1) The analytical result of kuromamin chloride agreed with that of chrysanthemin chloride $C_{21}H_{21}O_{11}Cl+1^1/_2H_2O$ in literature[3] ; and m.p. 182° of kuromamin picrate also agreed with that of chrysanthemin picrate.

(2) By characteristic colour reactions, the position of glucose was determined to be "3", namely kuromamin chloride turning violet with Na_2CO_3 ; blue with NaOH or $FeCl_3$. In these respects they were exactly identical with chrysanthemin chloride[4], but distinctly different from cyanenin (synthetic, 5-monoglucoside of cyanidin) chloride[5] which is known to give bright bluish green colouration with Na_2CO_3 and to be oxidised rapidly with $FeCl_3$. Further confirmative colour reactions with buffered solution[6] were observed. Then, the results with kuromamin chloride and natural specimen[7] of chrysanthemin chloride were quite identical, and agreed with the report on synthetic[8] chrysanthemin chloride, and were distinctly distinguished from those of cyanenin chloride[9] and natural specimen of cyanin chloride (3,5-diglucoside of cyanidin), and mecocyanin chloride, (3-gentiobioside of cyanidin chloride[10], natural and synthetic).

(3) Distribution number was determined by Willstätter's method ; the results being 19 (1st) and 19.15 (2nd) in agreement with those of the literature (natural[11], 19 and 19.5 ; synthetic[12], 19 and 19.1).

(4) As results of observations of absorption spectrum, kuromamin chloride and chrysanthemin chloride were also proved to be quite identical and were distinguished from those of cyanin chloride (natural, from dahlia and "shiso")[13].

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(3) Willstätter and Bolton, *Ann.*, **421** (1916), 146. S. Murakami, Robertson, and R. Robinson, *J. Chem. Soc.*, **1931**, 2670.

(4) S. Murakami, R. Robinson, and A. Robertson, *ibid.*, **1931**, 2668.

(5) Leon and Robinson, *ibid.*, **1932**, 2222.

(6) R. Robinson and A. Robertson, *Biochem. J.*, **23** (1929), 35.

(7) From flower of deep red *chrysanthemum indicum*.

(8) Murakami, Robertson, and Robinson, *J. Chem. Soc.*, **1931**, 2671.

(9) A. Leon and Robinson, *ibid.*, **1932**, 2222.

(10) Willstätter and Weil, *Ann.*, **412** (1916), 231. Grove, Inubuse, and Robinson, *J. Chem. Soc.*, **1934**, 1611.

(11) Willstätter and Bolton, *Ann.*, **412** (1916), 146.

(12) Murakami, Robinson, and Robertson, *J. Chem. Soc.*, **1931**, 2670.

(13) Kuroda and Wada, *Proc. Imp. Acad. Japan*, **11** (1935), 28.

(5) The aglucone of kuromamin was again verified exactly to be cyanidin, on comparing its properties (solubilities, colour reactions, and appearances, etc.) with those of our specimen of synthetic cyanidin chloride[14] (for which the writers thank Miss Yashiro for her kind help in a part of this synthesis) and of the aglucone from "Shiso" pigment and was also identified by the absorption spectrum[13].

(6) Upon the decomposition with acid, kuromamin yielded one mol each of cyanidin and glucose. The quantity of glucose was determined exactly by Pavy's method; the result was found to be in agreement (Found: 35. Calc.: 35%).

(7) Furthermore by Karrer's method[15] the position of glucose was also proved to be "3", namely by action of perhydrol.

(8) Kuromamin chloride was compared with the report on idaein chloride, 3-monogalactoside of cyanidin chloride[16] $C_{21}H_{21}O_{11}Cl+2^1/_2H_2O$; then they were actually distinguished from each other in their solubilities, quantities of water of crystallisation, and in their osazones (glucosazone from kuromamin, m.p. 203°; galactosazone, m.p. 186°).

Experimental.

Isolation of Kuromamin Chloride from Water-soluble Portion. When the beans (36 *l.*) from Hokkaido were immersed in cold water for several hours, a reddish purple aqueous solution was obtained. From the aqueous solution, bluish green precipitate was formed on addition of saturated aqueous lead acetate which was then filtered, dried on a tile quickly, powdered (yield, 0.5% of the beans) and triturated with cold glacial acetic acid. From the purple acetic acid solution thus obtained, a pure indigo blue lead salt of the pigment was precipitated upon the addition of several times its volume of ether (yield, 17 g.). When the above lead salt was treated by 2% CH_3OH–HCl, a red solution was obtained, and the chloride of the colouring substance was precipitated by addition of ether. And the chloride was triturated with a small quantity of absolute CH_3OH to remove easily soluble impurities. It crystallized out from dry CH_3OH–HCl in leaflets with a metallic lustre (Fig. 1) (yield, 0.4 g.). On analysis, the result agreed with a monoglucoside of cyanidin chloride (Found: C, 49.38; H, 4.73. Calc. for $C_{21}H_{21}O_{11}Cl+1^1/_2H_2O$: C, 49.30; H, 4.69%).

Hydrolysis of Kuromamin Chloride (from Water-soluble Portion) with Acid. The above kuromamin chloride (air dry, 0.1 g.) was dissolved in hot 0.1% aqueous HCl (6 c.c.), conc. HCl (6 c.c.) added, and the mixture was boiled for three minutes. On cooling, an aglucone (Fig. 2) crystallized out in reddish brown needles. Yield, 0.0642 g. (air dry, 64.2%. calc. 65.3%). It showed all the qualitative reactions of cyanidin chloride. The aglucone was recrystallized from 2% CH_3OH–HCl for analysis (Found: C, 52.79; H, 4.14. Calc. for

(14) A. Robertson and R. Robinson, *J. Chem. Soc.*, **1928**, 1526.
(15) Karrer and Meuron, *Helv. Chim. Acta*, **15** (1932), 1212.
(16) Willstätter and Mallison, *Ann.*, **408** (1915), 15.

cyanidin chloride $C_{15}H_{11}O_6Cl+H_2O$: C, 52.89; H, 3.82%). Micro-Zeisel estimation proved the absence of methoxyl groups in the aglucone.

Sugar. (1) *Estimation.* The above filtrate removed from the aglucone was neutralized with alkali carefully, evaporated on the water bath to dryness, then dissolved again in water, and filtered to remove completely any insoluble matter, and was dried on the water bath; the dry matter dissolved in H_2O (pale yellow solution), was made up to 100 c.c. of about 10% NH_3 with conc. NH_3 and the sugar estimated with Pavy's solution.

(2) *Osazone.* The resulting acid solution obtained upon decomposition of kuromamin chloride with 20% aqueous HCl was neutralized with alkali carefully and dried. The dry matter was dissolved in water and filtered. When the filtrate was heated with $C_6H_5NH\text{-}NH_2\cdot HCl$ and sodium acetate, glucosazone was formed: washed with CH_3OH, and ether, m.p. 205°, both alone and after admixture with the authentic specimen.

Isolation of Kuromamin Chloride from Water-insoluble Portion. The dry seed-coat, after the removal of the water-soluble pigment, was treated with 0.5% CH_3OH–HCl and to the resulting red solution, methyl alcohol solution of lead acetate was added drop by drop, and the bluish purple lead salt of the pigment was collected after removing the initial white precipitate of lead chloride. The purification of both the above lead salt and chloride of pigment was carried out as in the case of the water-soluble pigment. The chloride (0.5 g.) thus obtained was recrystallized from dry CH_3OH–HCl twice. The kuromamin chloride separated in leaflets with green metallic lustre. (Found: C, 49.24; H, 4.43. Calc. for $C_{21}H_{21}O_{11}Cl+1^1/_2H_2O$: C, 49-30; H, 4.69%.)

Hydrolysis with Acid. When the acid decomposition of the glucoside (from water-insoluble portion) (0.1 g.) was carried out as previously mentioned, cyanidin chloride (0.065 g.) separated in brown-red needles. Yield, 65%; calc. 65.3%. For analysis, the aglucone was recrystallized from 2% CH_3OH–HCl (Found: C, 52.70; H, 3.62. Calc. for $C_{15}H_{11}O_6Cl+H_2O$: C, 52.86; H, 3.82%. Estimation of sugar: Found: 34.05. Calc.: 35.22%).

Direct Isolation of Kuromamin Chloride from "Kuromame" from Hokkaido. The seed-coats were separated from the beans by the help of an electric fan, grinding in a hand mill at room temperature. They were then immersed in 2% CH_3OH–HCl for three hours, and into the resulting red solution, methyl alcohol solution of lead acetate was added drop by drop in order to precipitate the lead salt of pigment. On carrying out the subsequent treatment as already mentioned, the glucoside crystallized out; 1.5 g. of the crystalline chloride was derived from 8 *l.* of beans or 370 g. of seed-coat, showing a notable increase in the yield, hence the advantage of the present method (over the one employed formerly when beans were first immersed in water). (Found: C, 49.21; H, 4.79. Calc. for $C_{21}H_{21}O_{11}Cl+1^1/_2H_2O$: C, 49.30; H, 4.60%.) The conversion of the glucoside led to a quantitative yield of crystalline aglucone (Found: C, 52.72; H, 3.62. Calc. for cyanidin chloride $C_{15}H_{11}O_6Cl+H_2O$: C, 52.92; H, 3.82%).

Isolation of Kuromamin Chloride from "Kuromame" from Mukden. The seed-coat (550 g.) of beans from Moukden was treated with 2% CH_3OH–HCl directly and purified by the foregoing method. The glucoside obtained in crystals with a green metallic lustre was decomposed into one molecule each of cyanidin chloride and glucose, and analytical results of both the glucoside (Found: C, 49.02; H, 4.59. Calc.; C, 49.30; H, 4.69%) and the aglucone (Found: C, 52.51; H, 3.46. Calc.: C, 52.94; H, 3.82%)

agreed with cyanidin chloride-3-monoglucoside. 0.5 g. of the crystalline glucoside was derived from 550 g. of seed-coat.

Isolation of Kuromamin Chloride from "Kuromame" from Shing Tai Tzu. Seed-coat of beans from Shing Tai Tzu was treated under the same condition as that from Mukden with the same results: Analytical results of both the glucoside (Found: C, 48.98; H, 4.55%) and the aglucone (Found: C, 52.87; H, 3.97%) agreed with 3-monoglucoside of cyanidin chloride. 0.5 g. of kuromamin chloride was derived from 580 g. of seed-coat.

Kuromamin Picrate. Kuromamin chloride was dissolved in 0.05% aqueous HCl, and saturated aqueous picric acid was added. In every respect the picrate that separated as a deep brownish-red prisms with bronze glance in mass (decomposition point, 190–192°), was found to be identical with chrysanthemin (cyanidin-3-monoglucoside) picrate.

The Alkali Fusion of Kuromamin Chloride. Kuromamin chloride (1 g.) was fused with KOH (3 g.) and H_2O (small quantity) at 203°. After cooling, the product was dissolved in water, acidified with conc. HCl, extracted with ether, and was evaporated. From the ethereal residue, a lead salt was precipitated by the addition of lead acetate. The lead salt filtered was decomposed with dilute H_2SO_4 and extracted with ether; the ethereal solution was treated with animal charcoal, and evaporated. When the residue was purified with hot water, protocatechuic acid crystallized out in white needles; m.p. 193°, both alone and after admixture with an authentic specimen (the quantity was not enough for analysis). The filtrate from the lead precipitate was treated with dilute H_2SO_4; after removing $PbSO_4$, the filtrate was extracted with ether. From the ethereal solution, phloroglucinol was obtained in white long needles; m.p. 210°, both alone and after admixture with an authentic specimen (Found: C, 44.45; H, 6.26. Calc. for $C_6H_6O_3+2H_2O$: C, 44.44; H, 6.17%).

The Oxidation of Kuromamin Chloride with H_2O_2. To the chloride (1 g.) dissolved in 1% aqueous Na_2CO_3 (80 c.c.) 3% aqueous H_2O_2 (80 c.c.) was added and the mixture was left at room temperature for three hours, then acidified with H_2SO_4 and extracted with ether. From the ethereal extract protocatechnic acid was isolated in white needles; m.p. 193°, both alone and after admixture with the authentic specimen. (Found: C, 48.97; H, 4.75. Calc. for $C_7H_6O_4+H_2O$: C, 48.83; H, 4.65%.)

The Position of Sugar. Kuromamin chloride (0.3 g.) was dissolved in hot H_2O (3.5 c.c.) and after cooling, into the solution, 30% H_2O_2 (2.5 c.c.) was added and the mixture left at room temperature. When yellow coloured solution thus obtained, was neutralized with 2N NaOH very carefully, the excess of H_2O_2 was decomposed with Pt-black, and the whole was dried by distillation in vacuum. From the aqueous solution of the residue, glucosazone (m.p. 205°, both alone and after admixture with the authentic specimen) was obtained by heating with $C_6H_5NH{\cdot}NH_2{\cdot}HCl$ and sodium acetate (yield, 0.05 g.). In this result, the position of glucose was proved to be "3". The filtrate from the above osazone was treated as in the case of shisonin (see following pages), however, no osazone from position "5" has been formed.

Preparation of Chrysanthemin Chloride from Chrysanthemum. The fresh dark red flowers were treated with 2% CH_3OH–HCl and from the resulting red solution, a lead salt was precipitated by the addition of lead acetate. The lead salt was also converted into chloride as usual; the raw chloride dissolved in 0.05% aqueous HCl was converted into picrate as previously mentioned. And the picrate was reconverted into chloride by aid

of 2% CH_3OH-HCl, and was purified as in the case of kuromamin chloride, then chrysanthemin chloride crystallized out in leaflets with green metallic lustre and was found to be quite identical with kuromamin in every respect.

Experiments with Buffered Solution. Colour reactions in a range of buffered solution of graded *p*H were examined. The method of the Robertson and Robinson[14] was applied and the numbers refer to solutions of *p*H from 3.2 (1) to 11.0 (14) and then to more alkaline solution of unknown *p*H. The chloride of kuromamin and natural chrysanthemin gave quite identical results as follows: (1) Salmon-red; (2) salmon-red, fading; (3) bluish-red, fading; (4) bluish salmon-red to pink fading; (5) pink; (6) brown-violet; (9) (10) (11) brown-violet-red (keeping considerably); (13) (14) brown-violet; (15) violet; (16) bluish-violet.

Distribution Number. Amyl alcohol for this experiment was purified as follows: commercial amyl alcohol was washed with 0.5% aqueous HCl several times, then washed with water to remove a trace of acid and distilled (b.p. over 110°). Kuromamin chloride (air dry, 0.01 g.) was dissolved in 0.5% aqueous HCl (50 c.c.) and was shaken with the above amyl alcohol. The operation was repeated twice. After standing the amyl alcoholic layer was kept for use. The preparation of standard solution: kuromamin chloride (0.0019 g., air dry) was dissolved in hot 2% CH_3OH-HCl (2 c.c.), to the solution, amyl alcohol was added and the whole made up to 50 c.c. and was used as standard. The result of 1st operation; 0.0019 g. in amyl alcohol layer, distribution number 19; 2nd: 0.00155 g. in amyl alcohol layer, distribution number 19.15.

The Colour Reactions with Buffered Solutions. The three specimens, kuromamidin, shisonidin (17) and synthetic cyanidin chlorides gave the identical results. (1) Red, pink in 30 seconds; (2) bluish red, colourless in 30 seconds; (3) reddish violet, colourless in 30 seconds; (4) blue reddish violet, colourless in 30 seconds; (5) permanganate, colourless in 1 hour; (6) bluer than (5) permanganate in 30 seconds; (9) violet red, deep permanganate in 30 seconds.; (10) similar but a little bluer; (11) violet blue; (13) dark blue violet dichroic; (14) similar to (13); (15) dark blue violet; (16) blue, dark yellowish gray in 1 hour.

Absorption Spectra of Kuromamin, Chrysanthemin, Kuromamidin, and Synthetic Cyanidin Chloride. Photographs were taken for each substance dissolved in CH_3OH (N/10000), with iron arc as the light source. They were reproduced in another paper.[17]

The authors desire to thank the Imperial Academy for a grant, and Viscount Masatoshi Okochi, the President of the Institute, for his kindness for obtaining samples of the beans from Manchuria.

II. Shisonin, The Colouring Matter of "Shiso".

The pigment of "Shiso" leaves (*Perilla Ocimoides L. var Crispa Benth*)[18] is extensively used for colouring "Umeboshi" which is a kind of plum pickle favoured throughout Japan. The chemical study on this pigment was made

(17) Kuroda and Wada, *Proc. Imp. Acad. Japan*, **11** (1935), 189.

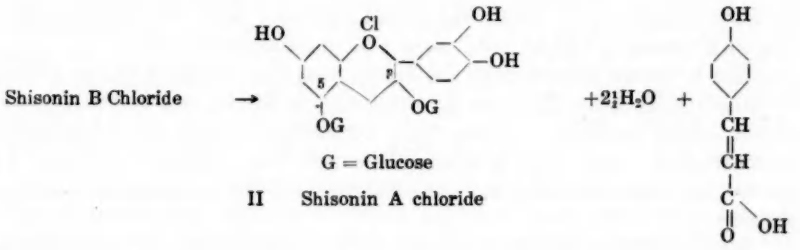
(18) Japanese special name "Chirimen Shiso".

by Dr. Kaoru Kondo,[19] a crystalline pigment "perillanin" was isolated and considered to be delphinidin-mono-glucoside combined with protocatechuic acid.

The present authors have undertaken the study of the anthocyan pigment obtained from the leaves cultivated in Tokyo, and some interesting new observations were made.

From "Shiso" leaves, a pigment which was named shisonin by the authors, was isolated as chloride. After several investigations shisonin was shown to be a mixture of glucosides, shisonin A and another new glucoside shisonin B. Shisonin A was isolated in a crystalline state as its chloride from the shisonin chloride by use of a suitable solvent. Shisonin B chloride was confirmed to be a compound of shisonin A chloride and *p*-coumaric acid, because the above two components were isolated, when shisonin B chloride was treated with cold alkali in H_2 atmosphere.

Shisonin A chloride was identified to be cyanin chloride, 3,5-diglucoside of cyanidin (II) in every respect.



G = Glucose

II Shisonin A chloride

For the direct comparisons, cyanin chloride was prepared from dahlia.[20] Appearances of crystals obtained in both cases under similar conditions were quite identical rhombic plates (Fig. 3) or fine needles (Fig. 4), m.p. (d.p.) being 195° as cyanin chloride. Moreover all the colour reactions, solubilities (except that, it was almost insoluble in cold water, or in dilute aqueous HCl, differing in this respect from mecocyanin[21]), and the analytical results ($C_{27}H_{31}O_{16}Cl+2^1/_2H_2O$)[22] were in agreement.

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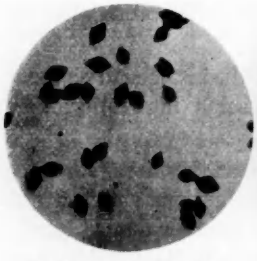
(19) *J. Pharm. Soc. Japan*, **51** (1931), 254.

(20) Kōzō Hayashi, *J. Bot. Japan*, **47** (1933), 396.

(21) Mecocyanin chloride, 3-bioside of cyanidin chloride $C_{27}H_{31}O_{16}Cl\cdot 3H_2O$: Willstätter and Weil, *Ann.*, **412** (1916), 231. A. Leon and R. Robinson *J. Chem. Soc.*, **1931**, 2737.

(22) Willstätter and Nolan, *Ann.*, **408** (1915), 1. Willstätter and Mallison, *Ann.*, **408** (1915), 147.



Shisonin A chloride from "Shiso"

Fig. 3.

Shisonin A chloride from "Shiso"

Fig. 4.

Shisonidin chloride from "Shiso"

Fig. 5.

Upon the decomposition with acid, from shisonin A chloride (m.p. 195°), one molecule of cyanidin chloride and two molecules of glucose were yielded quantitatively as anticipated. The estimation of the glucose was carried out by Pavy's method, in which the result agreed. And the positions of the glucose were proved to be "3" and "5" by Karrer's method.

The aglucone (brown crystals, Fig 5) was exactly proved to be cyanidin chloride ($C_{15}H_{11}O_6Cl+H_2O$), by its properties, analysis, and by the following decomposition products. When fused with alkali, it gave phloroglucinol and protocatechuic acid. The protocatechuic acid was obtained, however, in a better yield when the aglucone was oxidized with H_2O_2 in a sodium carbonate solution.

More confirmative colour reactions with buffered solution[14] were observed. The results with shisonin and cyanin chloride (from dahlia) were quite identical, and agreed with the report on synthetic cyanin chloride,[23] and were distinctly distinguished from those of chrysanthemin chloride, obtained from natural pigments, and also of cyanenin (synthetic, cyanidin 5-monoglucoside) chloride[9] and mecocyanin chloride[8] (natural).

As the results of estimation of distribution number and of observation of absorption spectrum, shisonin A was also proved to be quite identical with cyanin chloride.

In view of the above experimental results, the anthocyanin of "Shiso" is considered to be a mixture of shisonin A and shisonin B, the latter being a compound of *p*-coumaric acid and shisonin A; further study on the arrangement of *p*-coumaric acid in the interesting second glucoside shisonin B is progressing.

(23) R. Robinson and A. R. Todd, *J. Chem. Soc.*, **1932**, 2496.

Experimental.

Preparation of Sh sonin Chloride. A dry powder, which was cautiously prepared from the leaves (obtained from the vegetable market in Tokyo) was soaked in cold petroleum ether to remove the yellow pigment. On separating the yellow solution, it was then extracted with 2% CH_3OH-HCl. On addition of ether to the above resulting red solution a heavy red flocculent crude chloride of the colouring matter was precipitated and then, by dissolving this in H_2O and adding lead acetate the pigment was purified as lead salt. The lead salt was reconverted into chloride by aid of CH_3OH-HCl and ether by the similar method as previously mentioned for kuromamin chloride and purified.

The Isolation of Shisonin A Chloride. Amorphous shisonin chloride (2 g.) dissolved in water (50 c.c.) was treated with 4 N aqueous NaOH (50 c.c.) in H_2 and left for two hours at room temperature; then acidified with conc. HCl (calculated quantity) and extracted with ether. The residue (0.1 g.) of ethereal solution was washed with a small quantity of cold water, then was recrystallized from hot water by aid of animal charcoal twice. *p*-Coumaric acid, m.p. 207°, both alone and after admixture with the authentic specimen. (Found: C, 65.64; H, 5.06. Calc. for $C_9H_8O_3$: C, 65.64; H, 5.06%.)

When the above aqueous red solution, obtained free from *p*-coumaric acid, was left at room temperature, a dark brown coloured crystalline substance with metallic lustre gradually separated (the separation finished in 2 or 3 days); the dry matter (0.5 g.) thus obtained was washed with cold CH_3OH, was dissolved in hot 0.01% aqueous HCl (small quantity), to which an equal volume of 3% C_2H_5OH-HCl was added and left. Shisonin A chloride (decomposition point 195°) crystallized out in small rhombic plates (Fig. 3) with metallic lustre. It was recrystallized three times for analysis. (Found: C, 47.03; H, 5.54. Calc. for $C_{27}H_{31}O_{16}Cl+2^1/_2H_2O$: C, 46.86; H, 5.21%).

The Decomposition of Shisonin A Chloride with Acid. Shisonin A chloride (0.1024 g., air dry) was boiled with 20% aqueous HCl (5 c.c.) on the sand bath for three minutes, then cooled with ice; an aglucone crystallized out in reddish brown needles. Yield, 0.05 g. (air dry, 48.81%, calc. 49.2%). It showed all the qualitative reactions of cyanidin chloride. For analysis, a specimen was recrystallized from 2% CH_3OH-HCl. (Found: C, 52.72; H, 4.06. Calc. for cyanidin chloride $C_{15}H_{11}O_6Cl+H_2O$: C, 52.86; H, 3.82%). Micro-Zeisel estimation proved the absence of methoxyl groups in the aglucone.

Sugar. (1) *Estimation.* Crystalline shisonin A chloride (0.0985 g.) was boiled with 2)% aqueous HCl for 3 minutes. After cooling, the filtrate removed from the aglucone was treated as in the case of kuromamin and sugar was estimated by Pavy's method (Found: sugar, 50.44. Calc. for $C_{27}H_{31}O_{16}Cl+2^1/_2H_2O$: 52.10%).

(2) *Osazone.* Glucosazone from the resulting acid solution obtaind by acid hydrolysis of shisonin A chloride was formed in a similar method to the case kuromamin chloride.

(3) *The position of sugar.* Shisonin A chloride (0.3 g.) was treated with 30% H_2O_2 as in the case of kuromamin and glucosazone from position "3" was obtained, m.p. 205°, 0.04 g. The filtrate from the above osazone was heated with 15% aqueous HCl on the water bath for $1^1/_2$ hours, then filtered. The filtrate was neutralized with alkali and dried in vacuum. From the residue, glucosazone from position "5" was isolated by aid of $C_6H_5NH{\cdot}NH_2{\cdot}HCl$ and sodium acetate as usual. After purifying, yield 0.06 g.; m.p. 203°, both alone and after admixture with the authentic specimen.

Isolation of Shisonin A Chloride by the Use of Solvent. When amorphous shisonin chloride (5 g.) was warmed with absolute CH_3OH on the water bath and left for a few days, a pigment free from *p*-coumaric acid (microscopic crystals upon treatment with CH_3OH) was separated (dry matter 1.5 g.); this was sucked. This crystallized out in small rhombic plates (decomposition point 195°) with golden metallic lustre, when the dry matter was dissolved in hot 0.5% aqueous HCl and an equal volume of 3% C_2H_5OH–HCl was added. Recrystallized twice for analysis (Found : C, 46.74; H, 5.42. Calc. for $C_{27}H_{31}O_{16}Cl+2^1/_2H_2O$: C, 46.86; H, 5.21%.) From the compound, an aglucone was produced. (Found : C, 52.84; H, 4.06. Calc. for $C_{15}H_{11}O_6Cl+H_2O$: C, 52.86; H, 3.82%.)

Alkali Fusion of Shisonin A Chloride. Shisonin chloride (0.7 g.) was fused with KOH (2.1 g.); from the product, phloroglucinol (m.p. 207°) and protocatechuic acid (m.p. 196°, both alone and after admixture with the authentic specimen) were obtained.

The Oxidation of Shisonin A Chloride with H_2O_2. The oxidation with 3% H_2O_2 was similarly carried out as in the case of kuromamin; protocatechuic acid was isolated in good yield, m.p. 196°. (Found : C, 48.90; H, 4.55. Calc. for $C_7H_6O_4+H_2O$: C, 48.83; H, 4.65%.)

Cyanin Chloride from Dahlia. The dark coloured flowers of dahlia ("Chishima", "Ubatama", "Black diamond" about 100 g.) was immersed in 2% CH_3OH–HCl (160 c.c.) in cold for three hours. When the resulting red solution was concentrated at 35° under reduced pressure and left, the pigment crystallized out in needles. It was filtered, dried, and to the solution of the dry matter dissolved in 0.01% hot aqueous HCl (1 part), 3% C_2H_5OH–HCl (1 part) was added. Cyanin chloride crystallized in small rhombic plates with golden lustre (decomposition point 195°). To remove a trace of monoglucoside, the above chloride was dissolved in 0.5% aqueous HCl saturated previously with *n*-butyl alcohol and was shaken with butyl alcohol, saturated with 0.5% aqueous HCl twice, and then with isoamyl alcohol. Now, the aqueous layer was warmed and 3% C_2H_5OH–HCl was added. Pure cyanin chloride was isolated from the solution.

Another Comparison of Shisonin A and Cyanin Chloride. All the apparent characters of the specimens were identical and they furnished solutions (aqueous and alcoholic) having the same colour and behaviour under all conditions. All the ordinary reactions, the colours with Na_2CO_3 (blue) and aqueous $FeCl_3$ (violet) were observed identical.

The colour reactions in a range of buffered solutions were investigated and the same results were obtained as follows: (1) Rose, fading; (2) (3) bluish rose, colourless in 30 seconds; (4) cherry red, fading; (5) permanganate fading less rapidly; (9) more intense and more stable; (9) (10) (11) reddish-violet; (13) violet, fading; (14) blue violet, fading; (15) (16) blue, fading rapidly.

Comparison of Distribution. Shisonin A chloride (10 mg.) was dissolved in 0.5% aqueous HCl (50 c.c.) previously saturated with *n*-butyl alcohol. A similar solution of cyanin chloride (from dahlia) was prepared and both solutions were shaken twice with *n*-butyl alcohol (50 c.c. each time) previously saturated with 0.5% aqueous HCl. Each butyl alcohol layer was matched colorimetrically and was found to be identical.

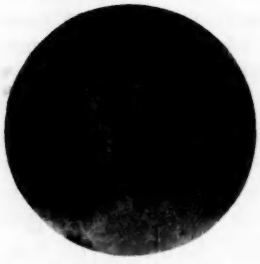
Absorption Spectra of Shisonin A, Cyanin (from Dahlia) and Shisonidin Chloride. Photographs were taken for each substance dissolved in CH_3OH (N/10000), with iron arc as a light source. They were reproduced in another paper.[24]

(24) Kuroda and Wada, *Proc. Imp. Acad. Japan*, **11** (1935), 189.

III. Nasunin, Colouring Matter of "Nasu".[25]

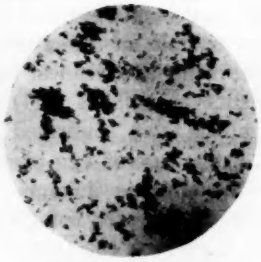
The vegetable fruit of egg-plant (*Solanum Melongena L. var erculentum Ness*) is not only a popular and useful vegetable food material from summer to autumn Japan, but the colour of its epidermis is noted for the beautiful dark purple which is taken as a standard, in dyeing from the olden time, being called as "Nasu blue." As cares are taken even in cooking to preserve this colour unaffected, the authors have been attracted to the study of the pigment. As the colour was extremely delicate and changeable it called for absolutely tedious methods with a special precautions to isolate the pigment. After preliminary tests, as the bright colouring matter of "Nasu" was shown to belong to an anthocyanin, the treatments were carried out by using the lead salt method accordingly.

The isolation of "Nasu" pigment in a crystalline state, was extraordinarily difficult; however, after several experiments, a new crystalline glucoside which was named nasunin by the authors was successfully obtained as picrate (Fig. 6), and finally as chloride.



Nasunin Picrate from "Nasu"

Fig. 6.



Nasunin A chloride from "Nasu"

Fig. 7.

Nasunidin chloride from "Nasu"

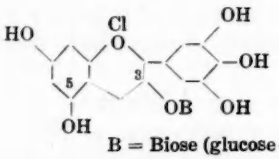
Fig. 8.

Then, as the results of careful investigations, nasunin was confirmed to be a compound of *p*-coumaric acid (1 mol) and a new glucoside which was named nasunin A by the authors was isolated as chloride, and was shown to be 3-bio-di-glucoside of delphinidin. The procedures are as follows: (1) Analytical results of nasunin chloride and picrate agreed with $C_{36}H_{37}O_{19}Cl+10H_2O$, $C_{42}H_{49}O_{26}N_3+4H_2O$, respectively. (2) The one component *p*-coumaric acid in nasunin was isolated quantitatively, when nasunin chloride was carefully treated with cold dilute aqueous NaOH in H_2. From the same glucoside, the above acidic component was also obtained by action of fused alkali. (3) On

(25) "Nasu" is the Japanese name of egg-plant.

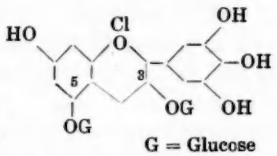
partial hydrolysis of nasunin chloride with cold 20% aqueous HCl, nasunin A as the another component in nasunin was isolated in crystalline state as chloride (Fig. 7). The analytical result ($C_{27}H_{31}O_{17}Cl+3H_2O$) was in agreement with diglucoside of delphinidin chloride. Decomposition of the glucoside with boiling HCl gave 1 mol of delphinidin chloride (Fig. 8) and 2 mols of glucose quantitatively.

Now one of the positions of glucose in nasunin was proved to be "3" by applying Karrer's[15] perhydrol method to nasunin chloride. Accordingly, the two formulae as di-glucoside are possible as indicated below:



B = Biose (glucose+glucose)

III Nasunin A chloride



G = Glucose

IV Awobanin chloride

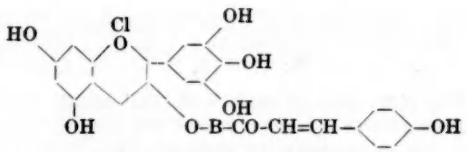
IV was obtained from "Awobana".[26] Although nasunin A in question corresponds well to the sample of IV from "Awobana" in almost every respect (absorption spectrum, appearance, and the results of analyses), there are some disagreements as follows: (1) Notwithstanding the fact that the glucoside of "Awobana" is confirmed to be 3,5-diglucoside by Karrer's perhydrol method, in the case of egg-plant, there are some experimental evidences against the glucose linkage "5". (2) Comparing the two substances in reactions in buffered solutions at 15 grades of pH[14], "Awobana" gives slightly more pink colouration than the other. (3) Solubilities of the two, in CH_3OH, H_2O, and HCl are also somewhat different, "Awobana" being less soluble. The decomposition point was a little different from that of "Awobana".

With such experimental facts in consideration, of the two proposed formulæ, III seems more probable.

Now, as to the manner of combination of one mol of p-coumaric acid, it may be linked as an ester to the biose at "3". A favourable example of such a view is violanin[27] (VI). Considering this example with the previously mentioned nasunin A which seemed to be 3-bioside of delphinidin, for the formula of nasunin chloride, V may be much more probable. Further studies will be made to confirm the present consideration.

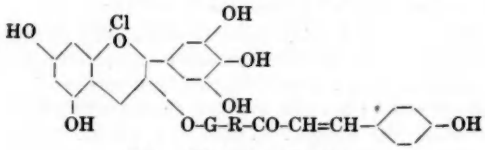
(26) See the foregoing paper.

(27) Karrer and Meuron, *Helv. Chim. Acta*, **16** (1933), 292.



V Nasunin chloride

B = Biose (glucose+glucose)



VI Violanin chloride

G = Glucose R = Rhamnose

Experimental.

Isolation of "Nasu" Pigment. The skins which were quickly peeled off from the fresh fruits were immediately immersed in 3% CH_3OH–HCl. Then in a few hours, the solution which turned bright red was taken out, and to this, a methyl alcohol solution of lead acetate was added drop by drop; the resulting white precipitate, lead chloride, was previously removed, then the indigo blue salt of the pigment was sucked, washed well with cold water, dried on a tile quickly, and powdered (150 fruits yielded 15 g. of the lead compound). The lead salt thus obtained was converted into a chloride solution by treating again with 2% CH_3OH–HCl. From the solution, the chloride of the colouring matter was precipitated upon the addition of several times its volume of ether, as the reddish purple and crystalline powder (150 fruits yielded about 1.5 g. of the chloride).

From this material dissolved in methyl alcohol, the colouring matter was precipitated by the addition of ether, this process being repeated for the purification.

Nasunin Picrate. To the solution of amorphous nasunin chloride (5 g.) in hot 1% HCl, powdered picric acid (3 g.) was added, warmed on the water bath for a few minutes, and left at room temperature for few days, then a reddish picrate gradually crystallized out (5 g.). The picrate thus obtained was dried, powdered, triturated with ether carefully to remove picric acid, and then was recrystallized twice from hot aqueous solution of picric acid saturated in cold (yield 2.5 g.). The picrate separated in beautiful red slender needles (copper-red mass in dry state, Fig. 6); for analysis, the specimen was purified several times (Found: C, 46.85; H, 4.82. Calc. for $C_{42}H_{39}O_{26}N_3+4H_2O$: C, 46.96; H, 4.37%). It agreed with picrate of delphinidin diglucoside combined with 1 mol of *p*-coumaric acid.

Nasunin Chloride. To the solution of the above pure picrate (2 g.) in 2% CH_3OH–HCl, ether was added, then reddish purple coloured nasunin chloride was isolated. The quantity of picric acid obtained from the above mother liquor (mixture of CH_3OH and ether) was determined (Found: picric acid, 0.38 g. or 38%. Calc. for $C_{42}H_{39}O_{26}N_2+4H_2O$: 0.38 g. or 38%).

The chloride was purified several times from CH_3OH–HCl or dilute aqueous HCl; the appearance of the chloride was similar to the picrate. (Found: C, 44.03; H, 5.7; Cl, 3.33. Calc. for $C_{36}H_{37}O_{19}Cl+10H_2O$: C, 43.73; H, 5.7; Cl, 3.31%.)

The Decomposition of Nasunin Chloride with Cold Alkali. Nasunin chloride (0.1 g.) dissolved in water (2.5 c.c.) was treated with cold 16% aqueous NaOH (5 c.c.) and kept for $2^1/_2$ hours at room temperature in H_2. The product was acidified, extracted with ether. From the ethereal solution, *p*-coumaric acid (white crystal, m.p. 207°) was isolated quantitatively (Found: 0.015 g. or 15%. Calc. for $C_{36}H_{37}O_{19}Cl+10H_2O$: 16.6%. Found: C, 65.61; H, 4.64. Calc. for $C_9H_8O_3$: C, 65.85; H, 4.87%).

Alkali Fusion of Nasunin Chloride. Nasunin chloride (1 g.) was fused with KOH (2 g.) (compare, fusion of nasunidin). When the ethereal extract of the product was triturated with minimum quantity of water, *p*-coumaric acid was obtained from the water-insoluble part, purified from hot water; the acid was obtained in white needles, m.p. 208° (Found: C, 65.54; H, 5.15. Calc. for $C_9H_8O_3$: C, 65.85; H, 4.88%). Other phenolic products obtained from delphinidin were also found.

Decomposition of Nasunin Chloride with Acid. When nasunin chloride (0.1275 g.) was boiled with 20% aqueous HCl for three minutes, and was cooled, delphinidin chloride separated out in an amorphous state as in the acid hydrolysis of nasunin A. The filtrate obtained free from the above aglucone was extracted with ether to remove *p*-coumaric acid, and the sugar content in the acid solution was determined by Pavy's method (Found: sugar, 0.05083 g. or 39.47. Calc. for $C_{36}H_{37}O_{19}Cl+10H_2O$: 36.44%).

Nasunin A Chloride. The solution of nasunin chloride (1 g.) dissolved in cold 20% aqueous HCl was left for a few days at room temperature. A bluish purple precipitate gradually separated (0.3 g.), which was washed with 0.5% HCl, and dried; this was dissolved in a minimum quantity of 0.5% hot aqueous HCl and an equal volume of 3% CH_3OH–HCl was added. On leaving for some time, nasunin A chloride crystallized out in golden lustrous fine needles (Fig. 7). It was recrystallized twice (decomposition point 197°) for analysis (Found: C, 44.90; H, 5.30; Cl, 4.45. Calc. for $C_{27}H_{31}O_{17}Cl+3H_2O$: C, 45.25; H, 5.17; Cl, 4.6%).

Hydrolysis of Nasunin A Chloride with Acid. To the purified nasunin A chloride (0.1 g.) dissolved in hot dilute aqueous HCl an equal volume of conc. HCl was added and the mixture boiled for two minutes. On cooling in contact with ice, an aglucone separated out as an apparently amorphous, nearly black precipitate. It was filtered, washed well with 20% HCl, and dried. The amorphous product was dissolved in hot dry CH_3OH, touched with dry HCl, then an aglucone crystallized out in plates with green metallic lustre (Fig. 8) and was dried in the air. It showed all the qualitative reactions of delphinidin (Found: C, 46.09; H, 4.57. Calc. for delphinidin chloride $C_{15}H_{11}O_7+3H_2O$: C, 45.91; H, 4.57%).

Micro-Zeisel estimation proved the absence of methoxyl groups in the aglucone. A delphinidin chloride hydrate of this composition has not previously been isolated, but it was already observed that the quantity of water of crystallization in such a substance depends on the conditions of crystallization.

Sugar. (1) *Estimation.* The above filtrate removed from the aglucone was neutralized with alkali, dried on the water bath, then the sugar was determined by Pavy's method as previously mentioned (Found: sugar, 0.0502 g. or 50.2%. Calc. for $C_{27}H_{31}O_{17}Cl+3H_2O$: 50.28%).

(2) *Osazone.* Glucosazone from the resulting acid solution obtained upon decomposition of nasunin A chloride was formed in the similar method as in the case of kuromamin chloride.

(3) *The position of sugar.* Nasunin A chloride (0.3 g.) was treated with 30% H_2O_2 as in the case of kuromamin, and glucosazone from position "3" was obtained in a considerable quantity, m.p. 205°. The filtrate from the above osazone was treated as in the case of shisonin, however, osazone from the position "5" was not found distinctly.

Alkali Fusion of Nasunidin (Aglucone of Nasunin). Nasunidin chloride (0.8 g.) was fused with NaOH (2.5 g.) and a small quantity of water at 203°. After cooling, the product was acidified with HCl, extracted with ether, and was evaporated. From the ethereal residue dissolved in water, a yellowish brown lead salt was precipitated by addition of lead acetate. The lead salt was filtered (filtrate A), washed with water, decomposed with dilute H_2SO_4, and extracted with ether. The ethereal residue dissolved in small quantity of CH_3OH was methylated with $(CH_3)_2SO_4$ and 50% aqueous KOH in H_2; the reaction product was heated on the water bath to decompose the ester and to evaporate CH_3OH, then acidified, extracted with ether, evaporated, and the residue was again extracted with hot benzene. The benzene-soluble part was crystallized from hot water, then gallic acid trimethyl ether (m.p. 165°, both alone and after admixture with the authentic specimen) was isolated. From filtrate A treated with dilute H_2SO_4, phloroglucinol was isolated (m.p. 208°, both alone and after admixture with the authentic specimen). No *p*-coumaric acid was found in this decomposition.

Direct Comparison of Nasunin A and Awobanin A Chloride. Both specimens were recrystallized in the same way with a different result as follows: The compound was dissolved in a minimum quantity of 0.5% hot aqueous HCl and an equal volume of 3% C_2H_5OH–HCl was added. After cooling, nasunin A chloride crystallized out in fine needles with golden lustre, while the other separated in small hexagonal plates with golden lustre.

The colour reactions of the above two specimens in buffered solutions were compared. The colours given by the two pigments were almost identical except that nasunin A became blue at a lower *p*H than awobanin A. (1) Rose-pink, fading rapidly; (3) (5) bluer, fading rapidly; (4) bluish-pink, fading to colourless rapidly; (9) (10) blue-violet; (11) violet; (13) violet-blue; (15) deep blue.

Both specimens were very sparingly soluble (or insoluble) in cold water, alcohol, and dilute aqueous HCl but readily in hot dilute aqueous HCl. All the ordinary reactions, the colours with Na_2CO_3 (a bright pure blue) and alcoholic $FeCl_3$ (violet-blue) were observed identical.

In buffered solution the colour reactions of both specimens, namely the aglucones from nasunin and awobanin chlorides, gave quite identical results agreeing with those of delphinidin chloride in the literature. (1) red, pink in 80 seconds; (2) violet red. colourless in 30 seconds; (3) permanganate, colourless in 30 seconds; (4) similar to (3); (5) violet; (6) deep violet red; (9) blue violet; (10) similar to (9); (11) blue violet; (13) blue violet dichroic, pale yellow in $1^1/_2$ hours; (14) indigo blue, pale yellowish gray in $1^1/_2$ hours; (15) (16) similar to (14).

The authors desire to thank Professor R. Majima for the kindest advice throughout this work, the Imperial Academy for a grant, and Miss Sumi Matsumoto for a part of micro-analyses.

R. Majima Laboratory, the Institute of Physical and Chemical Research.

ÜBER EIN UMLAGERUNGSPRODUKT DES FUKUGETINS (FUKUGENETIN).

Von Masuo MURAKAMI und Tôsi IRIE.

Eingegangen am 19. November 1935. Ausgegeben am 28. März 1936.

Fukugetin ist ein Farbstoff, der in der Rinde von *Garcinia spicata* oder *Xanthocymus ovalifolia* aufgefunden wird. Wir[1] untersuchten seit längerem die chemische Konstitution (I) dieses Farbstoffes und konnten sie mit ziemlicher Sicherheit festlegen. Da Fukugetin in seinem Molekül eine aktive Gruppe, $-COCH-CH-$ enthält, wird es durch Alkalien oder Säuren leicht isomerisiert. Fukugenetin ist eines von seinen Isomeren. Über die Natur dieses Isomers stellten wir einige Untersuchungen an.

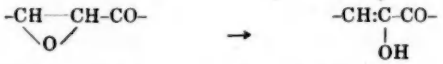
Beim Erhitzen des Fukugetins mit 50%iger Kalilauge erhielt J. Shinoda[2] zuerst Fukugenetin und stellte einige Derivate her. Für diese Isomerisierung ist Erhitzen mit 30%iger Kalilauge geeignet. Wir gewannen dabei in ziemlich guter Ausbeute ein saures Produkt, welches Roh-Fukugenetin genannt wurde und aus zwei Isomeren besteht, die aber nicht direkt voneinander getrennt werden konnten. Bei seinem Methylderivat konnte aber die zwei Isomeren gefasst werden. Das eine Produkt (A) schmilzt bei 208° und wird durch Methylierung[3] des reinen Fukugenetins auch gewonnen. Das andere (B) vom Schmp. 199–200° wird auch bei Methylierung aus dem später erwähnten Anhydro-isofukugenetin oder Triacetyl-anhydro-isofukugenetin erhalten. Nach der Zeiselschen Methoxyl-bestimmung scheint dieses Isomer 5 Methoxylgruppen zu enthalten, während aber die Imidomethylbestimmung die Existenz einer weiteren Methoxylgruppe zeigt. Wir stellten andererseits ein Methylderivat vom Schmp. 178.5–9° her, dessen Zeiselsche Bestimmung zu dem für 5 Methoxylgruppen berechneten Wert führte. Dieses Pentamethylderivat hat einen aktiven Wasserstoff und geht bei Methylierung in das obige Isomer B unter Verschwinden des aktiven Wasserstoffes über. Aus diesen Gründen müssen 6 Methoxylgruppen im B-Isomer[4] vorhanden sein. Beim Verseifen mit 10%igem alkoholischem Kali liefert es Tetramethylderivat vom Schmp. 258–260°, das eine Carbonsäure ist, also muss ein Methylester der Carbonsäure vorliegen.

(1) M. Murakami, *Proc. Imp. Acad. Japan*, **8** (1932), 500. M. Murakami und T. Irie, *ibid.*, **10** (1934), 568.

(2) (3) J. Shinoda, *J. Pharm. Soc. Japan*, **52** (1932), 1009.

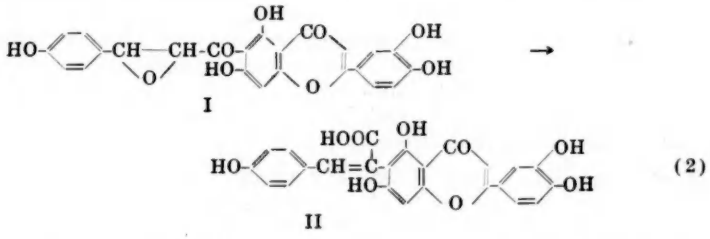
(4) J. Shinoda gab das Isomer als Pentamethylderivat an.

In der zweiten Mitteilung[5] berichteten wir die Umlagerung des Pentamethylfukugetins mit 5%igem alkoholischem Kali und erklärten sie mit der Reaktion (1).



(1)

Während die schwache Kalilauge zur Bildung der enolischen Hydroxylgruppe führt, verursacht die starke die Bildung der Carboxylgruppe. Da diese Umlagerungen den Keto-oxidoumlagerungen[6] sehr ähnlich sind, erklären wir sie mit Reaktion (2).



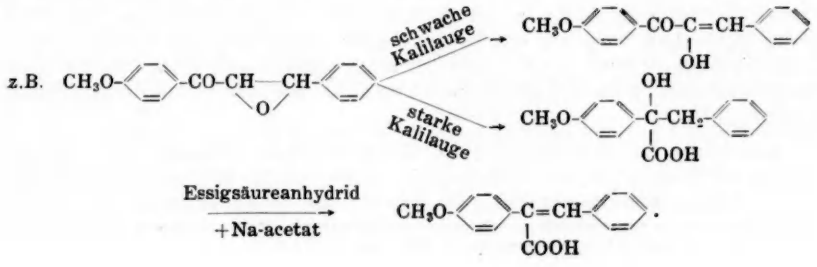
(2)

Mit Konstitution II lassen sich die obigen Eigenschaften des B-Isomers deutlich erklären. Methylderivat A hat eine mit B gleiche Molekularformel, also ist es wahrscheinlich eine Stereoisomer von B in Bezug auf die aufs neue gebildete Doppelbindung. Das rohe Fukugenetin enthält daher zweifellos neben dem von J. Shinoda isolierten Fukugenetin ein Isomer (Isofukugenetin), welcher das Methylderivat B gibt.

Isofukugenetin kann nicht aus dem rohen Fukugenetin isoliert werden, aber beim Erhitzen mit verd. Schwefelsäure verwandelt es sich in Anhydro-

(5) M. Murakami und T. Irie, *loc. cit.*

(6) O. Widman, *Ber.*, **49** (1916), 477. Jörlander, *Ber.*, **50** (1917), 406, 1458. M. Murakami und T. Irie, *loc. cit.*



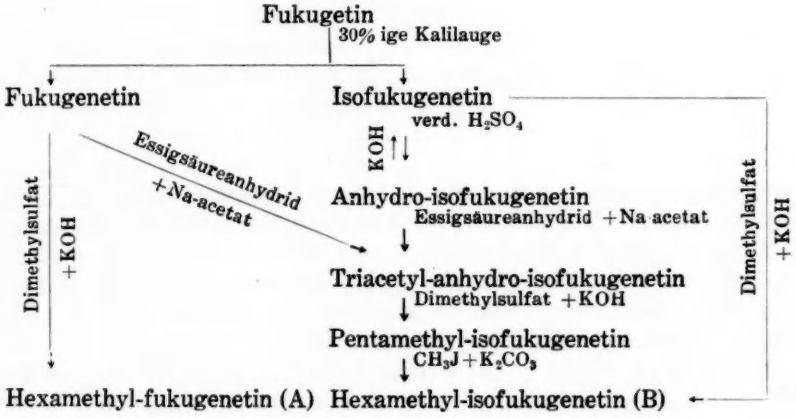
isofukugenetin[7], aus dem beim Behandeln mit verd. Kalilauge wieder Isofukugenetin rückgebildet werden kann, während Fukugenetin unverändert bleibt.

Da das Anhydro-isofukugenetin schon die saure Natur verliert, und bei der Acetylierung merkwürdigerweise nur Triacetyl-anhydro-isofukugenetin liefert, muss es noch dazu einen aktiven Wasserstoff unabhängig von der Laktonbildung verlieren.

Fukugenetin wird durch Erhitzen mit Essigsäureanhydrid und Natriumacetat in Anhydro-isofukugenetin verändert, während aber aus der Isofukugenetinreihe eine Rückveränderung bisher nicht möglich war.

In Tabelle 1 werden diese Veränderungen schematisch dargestellt.

Tabelle 1.



Versuche.

Roh-Fukugenetin. 5 g. Fukugetin wurden mit 50 g. 30%iger Kalilauge im Wasserstoffstrom 30 Minuten lang gekocht. Nach dem Ansäuern mit Salzsäure wurden die Produkte in Äther aufgenommen und die ätherische Lösung mit wässeriger Bicarbonatlösung geschüttelt. Aus der ätherischen Lösung wurde Fukugetin in kleiner Menge (0.2 g.) zurückgewonnen. Sein Pentamethylderivat schmolz bei 203–4°. Aus der Bicarbonatlösung wurde nach dem Ansäuern mit Salzsäure das rohe Fukugenetin erhalten. Ausbeute 2.1 g.

Acetylierung des rohen Fukugenetins. (Triacetyl-anhydro-isofukugenetin). 2 g. rohes Fukugenetin wurden mit 20 c.c. Essigsäureanhydrid und 3 g. Natriumacetat 2 Stunden lang gekocht. Dabei schieden sich gelbe Kristalle aus, die allmählich zu einem Kristall-

(7) Das Anhydro-fukugenetin von J. Shinoda.

brei erstarrten. Das Produkt wurde filtriert, zuerst mit Alkohol, dann mit Wasser gewaschen und aus Eisessig umkristallisiert. Schmp. 267°. Ausbeute 2 g.[8] Die alkoholische Lösung zeigte mit Eisenchlorid keine Färbung. (Gefunden: Acetyl, 23.13, 23.96, 23.98. Berechnet für $C_{24}H_{11}O_5(OCOCH_3)_5$: 23.28%. Gefunden: C, 64.89; H, 3.87. Berechnet für $C_{30}H_{20}O_{11}$: C, 64.73; H, 3.62%.)

Die Substanz wurde auch aus Anhydro-isofukugenetin gewonnen.

Darstellung des Anhydro-isofukugenetins aus rohem Fukugenetin. 3.5 g. rohes Fukugenetin wurden in 35 c.c. Äthanol gelöst, mit 20 c.c. verd. Schwefelsäure versetzt und 3 Stunden lang gekocht. Das enthaltene Isofukugenetin wurden dabei als Anhydro-isofukugenetin ausgeschieden. Es kristallisierte aus Pyridin in orangegelben Nadeln, die bei 380° noch nicht schmolzen. (Gefunden: C, 66.41, 66.67; H, 3.72, 3.54. Berechnet für $C_{24}H_{14}O_8$: C, 66.96; H, 3.28%.)

Isofukugenetin aus Anhydro-isofugenetin. Wenn man eine rote Lösung von 0.1 g. Anhydro-isofukugenetin mit 5 c.c. 10%iger Kalilauge bei gewöhnlicher Temperatur eine Weile stehen lässt, so schlägt die Farbe in gelb um. Beim Einleiten eines CO_2-Stroms schied sich aus der gelben Lösung ein gelber Niederschlag ab, der das Kaliumsalz der Carbonsäure war. Nach Ansäuern und Umkristallisieren wurde es in gelben, nadelförmigen Kristallen erhalten, die bei 380° noch nicht schmolzen. (Gefunden: C, 63.82; H, 3.77. Berechnet für $C_{24}H_{16}O_9$: C, 64.27; H, 3.60%.)

Methylierung des rohen Fukugenetins. 2.2 g. rohes Fukugenetin wurden in 40 c.c. Methanol und 40 g. Dimethylsulfat gelöst und allmählich mit Kalilauge (32 g. in 64 c.c. Wasser) versetzt. Das rohe Methylderivat, das aus zwei Isomeren besteht, wurde dabei ausgeschieden. Seine alkoholische Lösung zeigte mit Eisenchlorid keine Färbung. Die Trennung der beiden Isomeren wird in Tabelle 2 entworfen.

Kristalle A, B, und C waren identisch, und wurden auch bei der Methylierung des Fukugenetins erhalten (Hexamethyl-fukugenetin). (Gefunden: C, 67.93, 67.52; H, 5.64, 5.68. Berechnet für $C_{30}H_{28}O_9$: C, 67.64; H, 5.33%.)

Nadelförmige Kristalle vom Schmp. 199–200° wurden auch bei der Methylierung des Anhydro-isofukugenetins und des Triacetyl-anhydro-isofukugenetins erhalten (Hexamethyl-isofukugenetin). (Gefunden: C, 67.40, 67.70; H, 5.60, 5.63. Berechnet für $C_{30}H_{28}O_9$: C, 67.64; H, 5.33%. Gefunden als gesamte Werte bei Zeiselsche Methode und Imidomethyl-Bestimmung: OCH_3, 33.85. Berechnet für $C_{24}H_{10}O_3(OCH_3)_6$: 34.9%.)

Pentamethyl-isofukugenetin aus Triacetyl-anhydro-isofukugenetin. Die Methylierungsmethode war die gleiche wie bei rohem Fukugenetin. Wenn die Kalilauge in der Kälte sehr langsam hinzugefügt wurde, so wurde Hexamethyl-isofukugenetin (Schmp. 198°) gewonnen. Wenn die Kalilauge aber in der Wärme hinzugefügt wurde, so wurde Pentamethyl-isofukugenetin erhalten, das nach dem Umlösen aus Äthanol oder Essigsäureanhydrid bei 178.5–179° schmolz. (Gefunden: OCH_3, 30.86. Berechnet für $C_{24}H_{11}O_3(OCH_3)_5$: 29.9+%. Gefunden für 0.2042 g. Subst.: CH_4, 8.0 c.c. Berechnet für $C_{24}H_{10}O_3(OCH_3)_5OH : CH_4$, 8.8 c.c. Gefunden: C, 67.03; H, 5.26. Berechnet für $C_{29}H_{26}O_9$: C, 67.16; H, 5.06%.)

Bei der Methylierung nach der Claisenschen Methode lieferte die Substanz Hexamethyl-isofukugenetin.

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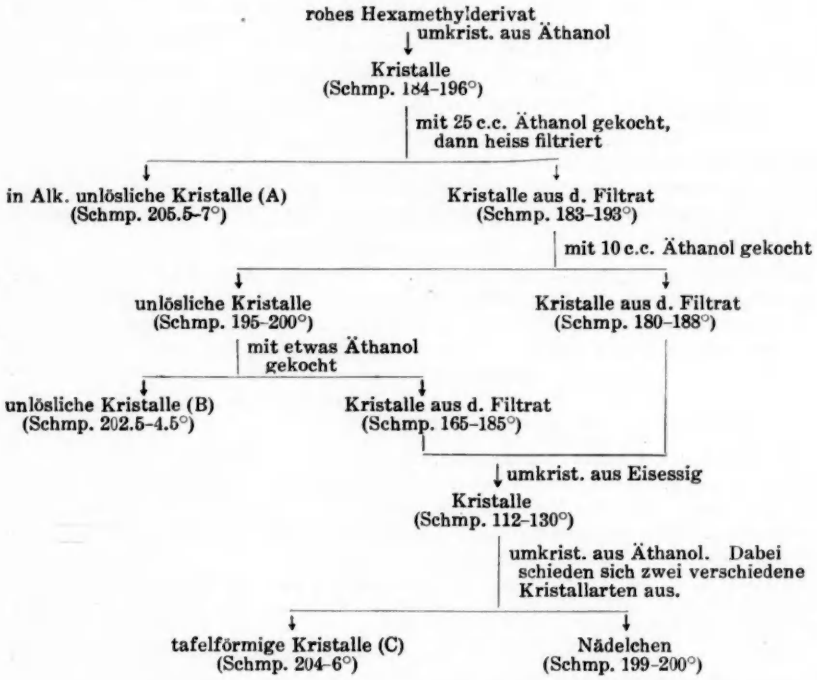
(8) Da sich alles Fukugenetin, das in dem rohen Fukugenetin enthalten ist, unter den gleichen Bedingung in Isofukugenetin umwandelte, wurde solch eine gute Ausbeute erzielt.

Tabelle 2.



Verseifung des Hexamethyl-isofukugenetins. 0.5 g. Hexamethyl-isofukugenetin wurden mit 10%iger alkoholischer Kalilauge 2 Stunden lang gekocht. Nach Abdestillieren des Alkohols im Vakuum wurde der Rückstand in Wasser gelöst, und dann mit Salzsäure gefällt. Nach Umkristallisieren aus Äthanol schmolz der Körper bei 258–260°. Seine alkoholische Lösung färbte Lackmuspapier rot. Er löste sich allmählich in Bicarbonatlösung. (Gefunden: C, 66.54, 66.50; H, 4.89, 4.98. Berechnet für $C_{23}H_{24}O_9$: C, 66.62; H, 4.79%.)

Zum Schluss möchten wir Herrn Prof. Rikō Majima für seine überaus freundliche Leitung bei der Ausführung dieser Untersuchung bestens danken und auch gleichzeitig der Kaiserlichen Akademie für ihre finanzielle Beihilfe unseren Dank aussprechen.

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ÜBER DIE STEREOISOMERIE DES 6-METHYL-DEKAHYDRO-CHINOLINS. (Vorläufige Mitteilung.)

Von Shin-ichiro FUJISE und Mitsuo IWAKIRI.

Eingegangen am 20. November 1935. Ausgegeben am 28. März 1936.

Die Stereochemie der hydrierten hetero-bicyclischen Verbindungen hat, seit der Entdeckung von *cis*- und *trans*-Dekahydrochinolin bzw. -isochinolin, beträchtliche Fortschritte gemacht[1]. H. Finger und W. Breiwieser[2] stellten 6-Methyl-dekahydrochinolin durch Reduktion von α-Cyan-6-methyl-chinolin mittels Natrium und Alkohol dar. Sie erhielten eine perhydrierte Base vom Schmp. 44°. Später gewann S. Yamaguchi[3] 6-Methyl-dekahydrochinolin von Schmp. 67° durch Reduktion von Benz-tetrahydrochinolin mit Natrium und Alkohol.

Die kristallisierten 6-Methyl-dekahydrochinoline, die die obigen Forscher erhalten hatten, zeigten verschiedene Schmelzpunkte. Im allgemein müssen monosubstituierte Dekahydrochinoline modellgemäss in je vier Racemformen auftreten; im Falle des 8-Oxy-dekahydrochinolins hat der eine von uns (F.) drei Racemformen isoliert[4]. Nun konnte man im Zweifel sein, ob bei den zwei oben beschriebenen 6-Methyl-dekahydrochinolinen der Fall einer Stereoisomerie vorliegte oder die niedrig schmelzenden Kristalle von einer verunreinigten Base herrühren können; da die stereochemische Untersuchung des 6-Methyl-dekahydrochinolins noch nicht ausgeführt ist, möchten die Verfasser hier die Resultate ihrer Versuche berichten.

Durch Hydrierung von 6-Methyl-chinolin in Eisessig bei 50° mit Platinoxyd und Wasserstoff, gewannen wir die vollständig hydrierte Base in fast quantitativer Ausbeute. Sie siedet bei 213–215° und das Destillat erstarrt bei guter Kühlung zu etwa dreisiebentel. Die Kristalle zeigten nach Umlösen in Petroläther einen Schmp. von 68–69°. Die flüssige Base wurde mit Bromwasserstoff-salz gereinigt und siedet nach Regeneration der freien Base bei 212–212.5°. Ganz allgemein ergaben der feste bzw. der flüssige Anteil zwei Reihen von Derivaten und die physikalischen Konstanten zeigten, dass die flüssige Base wie im Falle des Dekahydrochinolins, die *cis*-, feste die *trans*-Form sein muss.

(1) G. Wittig, „Stereochemie," S. 148 (Leipzig, 1930). S. Fujise, *Sci. Rep. Phys. Chem. Research, Japan*, **8** (1928), 161, 185; **9** (1929), 91.

(2) *J. prakt. Chem.*, **79** (1909), 445.

(3) *J. Pharm. Soc. Japan*, **43** (1923), 53.

(4) Vgl. dazu Fussnot (1).

	Siedp.(°C.)	d_4^{74}	n_D^{74}	EM_D
trans-6-Methyl-dekahydrochinolin (fest)	211.5–212	0.8694	1.46005	+0.69
cis-6-Methyl-dekahydrochinolin (flüssig)	212–212.5	0.8843	1.46514	+0.33

Schmelzpunkte der Derivate (°C.).

	Fest	Flüssig
Hydrochlorid	265	263–264
Hydrobromid	244–245	252–253
Goldchloriddoppelsalz	117–119	152–153
Platinchloriddoppelsalz	171.5–172.5	230 (zersetz.)
p-Nitrobenzoylverbindung	124.5–125	138–139
Benzoylverbindung	95–99	nicht kristallisiert

Das feste *trans*-6-Methyl-dekahydrochinolin wurde mit *d*-Bromcampher-sulfonsäure in die optisch aktiven Formen gespalten und zwar erhielten wir *d*-Form in reinem Zustand; sie schmolz bei 92–93°. $[\alpha]_D^{14.5°} = +4.8°$ (in Alkohol). Der Drehungswert ist nahezu gleich mit dem des *trans-d*-Dekahydrochinolins.

Das perhydrierte 6-Methyl-chinolin von Schmp. 44°, das H. Finger und W. Breiwieser isolierten, dürfte nach unseren Meinung unreine *trans*-Base gewesen sein.

Auf die experimentellen Einzelheiten soll später eingegangen werden.

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ÜBER DIE FARBSTOFFE IM HOLZTEILE DES "HINOKI"-BAUMES. I. HINOKITIN UND HINOKITIOL.

(Vorläufige Mitteilung.)

Von Tetsuo NOZOE.

Eingegangen am 20. November 1935. Ausgegeben am 28. März 1936.

Über die ätherischen Öle im Holze des "Hinoki"-baumes (*Chamaecyparis obtusa*, Sieb. et Zucc.), einem der wichtigsten Baumaterialien in Japan, insbesondere in Formosa, wurden bisher ziemlich eingehende Untersuchungen durchgeführt, während über die in demselben Holze enthaltenen Farbstoffe kaum Berichte vorliegen. Hirao[1] isolierte aus dem sauren Teile des ätherischen Öles des Formosanischen "Hinoki"-holzes eine ungesättigte Fettsäure, Chamaensäure von der Formel $C_{10}H_{16}O_2$. Bei der Oxydation dieser Säure mit Ferrichlorid erhielt er Hinokitin, einen roten Farbstoff vom Schmelzpunkt 250–1°, für den die Molekularformel $C_{30}H_{34}O_{10}$ angenommen wurde. Er schrieb übrigens die Farbe des "Hinoki"-öles, so wie des "Hinoki"-holzes diesem Farbstoff zu, wofür aber die Bestätigung noch gänzlich fehlt.

Früher als Hirao isolierten Tsuchihashi und Tasaki[2] aus dem Formosanischen "Hinoki"-öl eine Säure $C_9H_{16}O_2$ und ein Phenol $C_{10}H_{14}O_2$. Da die physikalischen Konstanten dieser Säure ganz verschieden von denen der Chamaensäure sind, untersuchten Kafuku und der Verfasser dieser Arbeit[3] den sauren Teil des ätherischen Öles im Holze, sowie in den Blättern und Wurzeln des "Hinoki"-baumes, um über diese Diskrepanz der physikalischen Konstanten sichere Daten zu gewinnen. Unsere Ergebnisse stimmten aber im wesentlichen mit den von Tsuchihashi und Tasaki[2] überein, und liessen überdies erkennen, dass die so genannte Chamaensäure und die von uns erhaltene phenolische Substanz die gleichen physikalischen Konstanten miteinander gemein haben.

Der nach der üblichen Weise abgetrennte und anfangs als rein angenommene saure und phenolische Teil zeigt jeweils eine identische Farbenreaktion mit Ferrichlorid, aber nach den näheren Untersuchungen hat die Säure selbst nichts mit der betreffenden Farbenreaktion zu tun, sondern nur die phenolische Substanz färbt sich unter Bildung des Hinokitins rot.

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(1) *J. Chem. Soc. Japan*, **47** (1926), 666, 743.
(2) *Report of Goverm. Research Inst. Formosa*, **1** (1920).
(3) Dieses Bulletin, **6** (1931), 40. Zum Teil noch unpubliziert.

Der unter Bildung von Hinokitin völlig vom phenolischen abgetrennte saure Teil weist in seinen physikalischen Konstanten keinen grossen Unterschied von demselben vor der Behandlung auf, zeigt aber im Gegensatz zu dem letzteren die Farbenreaktion nicht, und die eingehenden Untersuchungen lassen erkennen, dass die Säure 1-Rhodinsäure $C_{10}H_{18}O_2$ ist.

Die Hauptfraktion des phenolischen Teiles entspricht nach Elementaranalyse und Titration einem einwertigen Phenol von der Formel $C_{10}H_{12}O_2$ oder $C_{10}H_{14}O_2$. Um die Funktion des zweiten Sauerstoffatomes des Phenols zu erklären, wurde die Substanz mit Alkohol- bzw. Keton-reagenzien behandelt. Sie reagierten sämtlich damit, aber die Reaktionsprodukte konnten nie kristallinisch erhalten werden. Die phenolische Substanz enthält auch keine Methoxylgruppe.

Wenn man die phenolische Substanz in der Anwesenheit von Natriumacetat mit einer Ferrichloridlösung behandelt, so kann man sehr leicht in guter Ausbeute Kristalle des oben erwähnten Hinokitins darstellen. Da es von grossen Vorteil schien, zur Aufklärung der Konstitution jener phenolischen Substanz das Hinokitin Prüfung zu unterziehen, wurde zuerst eine genauere Untersuchung darüber in Angriff genommen.

Hinokitin löst sich in Wasser, Pyridin, heissem Aceton, Chloroform und Benzol und ist in sonstigen gewöhnlichen Lösungsmitteln schwer löslich. Es bildet prachtvolle dunkelrote Kristalle vom Schmelzpunkt 251°, sublimiert im Hochvakuum schönen Nadeln und lässt sich allem Anschein nach fast unzersetzt destillieren. Selbst in einer sehr verdünnten Lösung ist es ziemlich intensiv rot gefärbt und hat zwei Absorptionsmaxima bei 584 und 540 $m\mu$ im sichtbaren Gebiet des Spektrums. Nach der Analyse ist seiner Formel nicht $C_{30}H_{34}O_{10}$, sondern $C_{30}H_{33}O_6Fe$, d.h. es enthält entgegen allen Annahmen Eisen.

Wenn man aus dem Hinokitin das Eisen entfernt, so erhält man wieder ein flüchtiges Öl, das der Formel $C_{10}H_{12}O_2$ entspricht und in seinen physikalischen, aber auch übrigen Eigenschaften mit der ursprünglichen phenolischen Substanz ziemlich gut übereinstimmt. Beim Behandeln dieses Öles mit Ferrichlorid erhält man quantitativ wieder das Hinokitin.

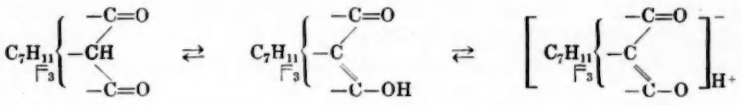
Das auf diese Weise mit dem Hinokitin in Beziehung stehende Öl wurde Hinokitiol genannt. Das Hinokitin ist also kein Oxydationsprodukt des Hinokitiols, sondern ein inneres Komplexsalz, Eisen (III)-Hinokitiolat. Die von uns abgetrennte und zuerst als rein angenommene phenolische Substanz war ebenso wie die Chamaensäure Hiraos[1] etwas 1-Rhodinsäure enthaltendes Hinokitiol. Die Beziehung zwischen dem Hinokitiol und Hinokitin ist also folgendermassen anzunehmen:

$$3C_{10}H_{12}O_2 + FeX_3 \rightleftarrows C_{30}H_{33}O_6Fe + 3HX.$$

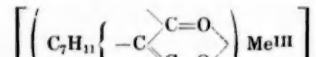
Über die Konstitution des über Hinokitin rein dargestellten Hinokitiols ist die Untersuchung noch im Gange. Mittels Alkohol-bzw. Keton-reagenzien erhaltene Derivate des Hinokitiols sind noch nicht kristallinisch erhalten worden. Immerhin konnten innere Komplexsalze desselben mit mehreren Metallen in gut kristallisiertem Zustand leicht hergestellt werden, worunter alle ausser denen der Alkalimetalle in Wasser unlösliche, in organischen Lösungsmitteln lösliche bzw. leicht lösliche neutrale Substanzen sind und allgemeine Eigenschaften eines neutralen inneren Komplexsalzes zeigen. Die inneren Komplexsalze des Hinokitiols mit zwei wertige Metallen bilden im allgemeinen mit zwei Mol organischen Basen kristallinische Verbindungen von konstantem Schmelzpunkt. Einige wichtige Metallkomplexsalze des Hinokitols seien im folgenden angegeben:

Metalle	Schmp.	Pyridin-deriv.	Chinolin-deriv.	Anilin-deriv.
$Cr^{\cdots}$	230°	—	—	—
$Fe^{\cdots}$	251°	—	—	—
$Co^{\cdots}$	208°	—	—	—
$Cu^{\cdot\cdot}$	177°	107°	96°	89°
$Ni^{\cdot\cdot}$	242°	210°		162°
$Co^{\cdot\cdot}$	210°	209°		113°
$Mn^{\cdot\cdot}$	>300°	>300°		
$Cd^{\cdot\cdot}$	>300°	>300°		
$Zn^{\cdot\cdot}$		164°		
$Mg^{\cdot\cdot}$	>300°	>300°		

Das Hinokitiol absorbiert bei katalytischer Reduktion 3–4 Mol Wasserstoff, die so erhaltene Substanz bildet im Gegenteil zum Hinokitiol nicht mehr innere Metallkomplexsalze, woraus folgt, dass das Hinokitiol eine ungesättigte 1,2- oder 1,3-Oxyoxo- oder Dioxoverbindung sein sollte. Die vergleichenden Studien zeigten aber, dass das Hinokitiol ein zwei Doppelbildungen enthaltendes monocyclisches 1,3-Diketon—wahrscheinlich mit einem Fünfring—ist, und folgendes Gleichgewicht vorliegen dürchte:

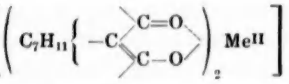


Zusammenfassend haben also Hinokitin und Metall-hinokitiol-Komplexsalze im allgemeinen folgende Formel I bzw. II und demnach die Verbindungen der Komplexsalze mit organischen Basen Formel III:

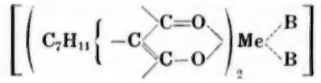


Hinokitin (Me = Fe)

I



II



III

Der Verfasser hat festgestellt, dass die rote Färbung des "Hinoki"-öles hauptsächlich dem Hinokitin zuzuschreiben ist; es ist aber gut möglich, dass das im "Hinoki"-öle gefundene Hinokitin aus dem im Öle vorkommenden Hinokitiol a posteriori, also z.B. aus dem Hinokitiol und dem Eisen des gebrauchten eisernen Gefässes, gebildet wurde. Da aber das Hinokitiol, eine mit Metallen ausserordentlich leicht Komplexsalze bildende Substanz, im "Hinoki"-holze vorkommt, ist es ganz leicht möglich, dass Metallhinokitiolate wie Hinokitin auch als eigentliche Farbstoffe des "Hinoki"-holzes selbst vorliegen. In dieser Hinsicht sind jetzt Versuche, die Farbstoffe des Hinokiholzes direkt zu trennen und rein zu erhalten, im Gange.

Es scheint noch nicht bekannt zu sein, dass eine fast farblose Substanz wie das Hinokitiol mit einem Metall unter Bildung eines Komplexsalzes schon als Farbstoff in der Natur vorkommt; das Hinokitin dürfte also zu einem neuen Typus der natürlichen Farbstoffe gehören.

Der Verfasser hat noch mikroskopisch festgestellt, dass auch im ätherischen Öle des "Benihi"-baumes (*Chamaecyparis formosensis*, Matsum.) das Hinokitiol vorkommt, und ist mit Rücksicht darauf, dass Hinokitiol, Hinokitin und mit ihnen verwandte Verbindungen in der Natur weitverbreitet sein dürften, augenblicklich mit Arbeiten weitere derartige Verbindungen aufzufinden beschäftigt.

Herren Prof. K. Kafuku ist der Verfasser für seine Leitung und den Herren Prof. R. Majima von der Universität zu Osaka und Prof. Y. Nakatsuka für die ihm gewährten Erleichterungen bei dieser Arbeit zu herzlichem Dank verpflichtet. Der Kaiserlichen Akademie spricht er auch seinen Dank für die finanzielle Unterstützung dieser Arbeit aus.

Organisch-chemisches Laboratorium der Universität, Taihoku.

ÜBER DIE LACCASE DES JAPANISCHEN LACKS. II. ÜBER DIE REAGIERBARKEIT DER LACCASE GEGEN POLYPHENOLE UND DIAMINE.[1]

Von Kunihiko SUMINOKURA.

Eingegangen am 26. November 1935. Ausgegeben am 28. März 1936.

Von den Polyphenole und Diamine oxydieren durch molekularen Sauerstoff bei Anwesenheit von Laccase nur diejenigen leicht, bei welchen die OH- oder NH_2-Gruppen in Ortho- oder Para-Stellung stehen, während dies die Meta-Verbindungen nur schwer tun, was früher bereits Bertrand[2] mitgeteilt hat und später von verschiedenen Autoren als richtig bestätigt wurde.

Ich behandelte 48 Phenole und Amine mit der Laccase des japanischen Lacks und Sauerstoffgas. Die bei meinen Versuchen gewonnenen Resultate finden sich in Tabelle 1. Am leichtesten oxydieren bei Anwesenheit der Laccase die *p*-Phenylendiamine (Dimethyl-*p*-phenylendiamin, *p*-Phenylendiamin), dann kommen die *o*-Dioxyphenole (Urushiol, Oxyhydrochinon, Brenzcatechin), die *o*-Phenylendiamine (*o*-Phenylendiamin, Adrenalin, Diamidophenol) und die Benzole mit einer Hydroxyl- plus einer Methoxyl-Gruppe. Die Meta-Verbindungen (Resorcin, Orcin, Phloroglucin, *m*-Phenylendiamin), die Benzole mit zwei Äthoxylgruppen (Hydrochinondiäthyläther) und die Benzole mit einer Hydroxyl- plus verschiedenen anderen Gruppen (Tyrosin, Tyramin, Thymol, Salicylaldehyd) oxydieren nicht. Obgleich Alizarin, Protocatechusäure und Dioxyphenylalanin Ortho-Dihydroxyl besitzen, oxydieren diese Verbindungen doch nicht. Hydrourushiol oxydiert nur schwer. Ebenso oxydieren das Methylenoxyd des Safrols und die aliphatischen Diamine gar nicht. Merkwürdig sind die Kresole; die, obgleich sie nur eine Hydroxyl-Gruppe besitzen, oxydieren sie doch etwas bei Anwesenheit der Laccase. Hier auch oxydieren nur Ortho- und Meta-Kresole, aber die Para-Verbindung nicht.

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(1) I. Mitteilung, *Biochem. Z.*, **224** (1930), 292-321.

(2) G. Bertrand, *Compt. rend.*, **122** (1896), 1132.

Tabelle 1.

Substanz	Konstitution	Oxyd. mit Laccase
Ortho-Verbindungen		
Brenzcatechin	C_6H_4(OH (1), OH (2))	+
Pyrogallol	C_6H_3(OH (1), OH (2), OH (3))	+
Urushiol	C_6H_3(OH (1), OH (2), $C_{15}H_{27}$ (3))	+
Hydrourushiol	C_6H_3(OH (1), OH (2), $C_{15}H_{31}$ (3))	+ (wenig)
Guajacol	C_6H_4(OH (1), OCH_3 (2))	+
Eugenol	C_6H_3(OH (1), OCH_3 (2), $CH_2CH{:}CH_2$ (4))	+
Adrenalin	C_6H_3($CH(OH)CH_2NHCH_3$ (1), OH (3), OH (4))	+
o-Kresol	C_6H_4(OH (1), CH_3 (2))	+ (wenig)
o-Phenylendiamin	C_6H_4(NH_2 (1), NH_2 (2))	+
3-Methoxy-4-oxy-phenyläthyl-methyl-keton		+
,, -octenyl-keton		+
,, -heptenyl-keton		+ (wenig)
,, -pentadecyl-keton		−
,, -nonyl-keton		−
,, -octyl-keton		−
,, -heptyl-keton		−
,, -hexyl-keton		−
Protocatechusäure	C_6H_3(COOH (1), OH (3), OH (4))	−

Tabelle 1. (*Fortsetzung.*)

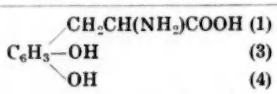
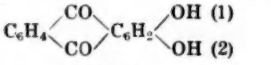
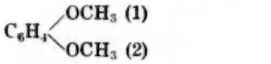
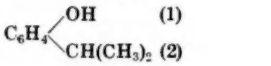
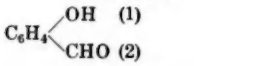
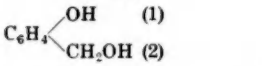
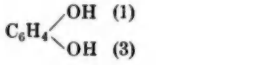
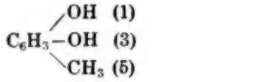
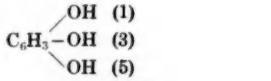
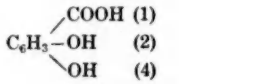
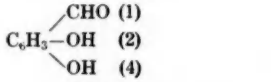
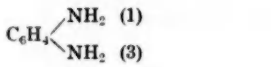
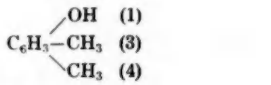
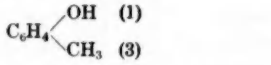
Substanz	Konstitution	Oxyd. mit Laccase
Dioxyphenylalanin		–
Alizarin		–
Veratrol		–
Thymol		–
Salicylaldehyd		–
Saligenin		–
Meta-Verbindungen		
Resorcin		–
Orcin		–
Phloroglucin		–
Dioxybenzoesäure		–
Dioxybenzaldehyd		–
m-Phenylendiamin		–
Xylenol		–
m-Kresol		+ (wenig)

Tabelle 1. (*Fortsetzung.*)

Substanz	Konstitution	Oxyd. mit Laccase
Para-Verbindungen		
Hydrochinon	$C_6H_4(OH\ (1), OH\ (4))$	+
Oxyhydrochinon-triacetat	$C_6H_3(OOCCH_3\ (1), OOCCH_3\ (2), OOCCH_3\ (4))$	+
Hydrochinonmonomethyläther	$C_6H_4(OH\ (1), OCH_3\ (4))$	+
Hydrochinondimethyläther	$C_6H_4(OCH_3\ (1), OCH_3\ (4))$	−
Hydrochinondiäthyläther	$C_6H_4(OC_2H_5\ (1), OC_2H_5\ (4))$	−
Diamidophenol-hydrochlorid	$C_6H_3(OH\ (1), NH_2{\cdot}HCl\ (2), NH_2{\cdot}HCl\ (4))$	+
p Phenylendiamin	$C_6H_4(NH_2\ (1), NH_2\ (4))$	+
Dimethyl-*p*-phenylendiamin	$C_6H_4(NH_2\ (1), N(CH_3)_2\ (4))$	+
,, -hydrochlorid	$C_6H_4(NH_2{\cdot}HCl\ (1), N(CH_3)_2\ (4))$	−
p-Kresol	$C_6H_4(OH\ (1), CH_3\ (4))$	−
Tyrosin	$C_6H_4(OH\ (1), CH_2CH(NH_2)COOH\ (4))$	−
Tyramin	$C_6H_4(OH\ (1), CH_2CH_2NH_2\ (4))$	−
Methylenoxyd-Verbindung		
Safrol	$CH_2(O,O)C_6H_3CH_2CH{:}CH_2$	−
Aliphatische Amine		
Äthylendiamin	$NH_2(CH_2)_2NH_2$	−
Putrescin-dihydrochlorid	$NH_2(CH_2)_4NH_2{\cdot}2HCl$	−
Cadaverin-dihydrochlorid	$NH_2(CH_2)_5NH_2{\cdot}2HCl$	−

Experimenteller Teil.

Nachdem Phenole bzw. Amine in einen Reaktionskolben (Abb. 1, a) aufgenommen worden, wurden einige c.c. Wasser oder Alkohol und 10 c.c. 1/3 Mol Phosphat-Puffer von *p*H 6.0 hinzugefügt. In der Kugel b wurde bei geschlossenem Hahn h eine Laccase-Lösung gebracht. Darauf wurde der Reaktionskolben mit der Gasbürette verbunden und in einen Thermostaten von 20.0°C. getaucht. Nachdem er evakuiert und darauf mit Sauerstoff gefüllt wurde, wurde der Hahn h geöffnet und der Reaktionskolben geschüttelt. Damit die Versuche unter konstantem Druck verlief, benützte ich die Petterson'sche Bürette.

Die meisten Substrate wurden in der Menge von 5/10000 g. Mol. verwendet, nur die Methoxylhydroxyl Ketone (Diese Ketone verdanke ich der Liebenswürdigkeit von Prof. Dr. H. Nomura.) der von 2/10000 g. Mol. Um die Reaktionsgeschwindigkeiten miteinander vergleichen zu können, wurde stets dasselbe aus dem japanischen Lack („Kiurushi" aus Saji, Tottori) hergestellte Laccasepräparat benützt.

Die Resultate, die sich bei den gegen Laccase indifferenten Substraten ergaben, sind hier nicht mitgeteilt.

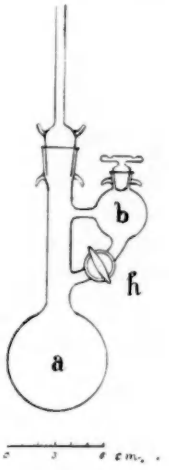


Abb. 1. Reaktionskolben.

Versuch 1. Substrat: Brenzcatechin 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 770.5 mm.

Tabelle 2.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	1.293 mg.	90 Min.	8.508 mg.
3	1.939	115	9.259
5	2.401	180	11.502
10	3.245	240	12.728
17	4.036	300	13.546
30	4.986	420	14.404
60	7.083	495	14.694
77	8.006	ca. 22 Stdn. (nicht geschüttelt)	15.947

Versuch 2. Substrat: Guajakol 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 767.4 mm.

Tabelle 3.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.407 mg.	120 Min.	4.624 mg.
3	0.499	180	5.885
5	0.578	240	6.726
10	0.801	270	6.858
15	1.077	360	7.173
30	1.760	480	7.751
60	2.890	540	7.974
90	3.849	ca. 23 Stdn. (nicht geschüttelt)	9.511
105	4.190		

Versuch 3. Substrat: Eugenol 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 767.6 mm.

Tabelle 4.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.486 mg.	120 Min.	6.833 mg.
3	0.644	190	7.227
5	0.854	244	7.332
10	1.406	300	7.503
15	1.879	422	7.858
30	3.403	476	7.989
35	3.916	481	8.002
60	5.519	508	8.160
90	6.504	ca. 23 Stdn. (nicht geschüttelt)	11.813

Versuch 4. Substrat: Hydrochinon 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 761.8 mm.

Tabelle 5.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.547 mg.	64 Min.	7.987 mg.
3	0.912	80	8.417
5	1.290	290	8.548
10	2.046	410	8.808
25	4.222	530	8.834
30	4.886	ca. 23 Stdn. (nicht geschüttelt)	13.095
60	7.792		

Versuch 5. Substrat: Adrenalin 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 759.8 mm.

Tabelle 6.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
5 Min.	1.261 mg.	180 Min.	15.854 mg.
15	2.378	240	17.673
30	3.704	360	19.194
60	6.121	480	20.129
84	7.914	570	20.818
120	10.630	ca. 23 Stdn. (nicht geschüttelt)	22.481
135	11.838		

Versuch 6. Substrat: Urushiol (destilliert) 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 765.0 mm.

Tabelle 7.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
3 Min.	2.395 mg.	180 Min.	13.190 mg.
9	5.587	240	13.464
17	8.767	300	13.752
30	11.292	360	13.936
45	11.881	420	14.145
60	12.195	ca. 21 Stdn. (nicht geschüttelt)	18.254
120	12.836		

Versuch 7. Substrat: Hydrourushiol 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 767.5 mm.

Tabelle 8.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.197 mg.	240 Min.	1.603 mg.
4	0.263	300	2.299
13	0.328	390	2.639
30	0.394	ca. 25 Stdn. (nicht geschüttelt)	3.143
60	0.736	30 Stdn. (von 25 bis 30 Stdn. geschüttelt)	4.452
120	1.051		

Versuch 8. Substrat: *o*-Phenylendiamin 5/100[illegible]. Mol. Laccase: 50 mg. Barometrischer Druck: 760.8 mm.

Tabelle 9.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.547 mg.	88 Min.	8.015 mg.
3	0.859	120	9.343
6	1.236	182	10.904
10	1.757	240	11.594
15	2.342	300	12.140
30	3.956	425	12.635
45	5.296	540	12.856
60	6.454	ca. 23 Stdn. (nicht geschüttelt)	14.639

Versuch 9. Substrat: *o*-Kresol 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 766.8 mm.

Tabelle 10.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
2 Min.	0.446 mg.	330 Min.	0.801 mg.
30	0.459	420	1.076
120	0.512	540	1.273
240	0.761		

Versuch 10. Substrat: *o*-Kresol 5/10000 g. Mol. Laccase: 200 mg. Barometrischer Druck: 765.9 mm.

Tabelle 11.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.432 mg.	240 Min.	1.965 mg.
10	0.642	330	2.279
60	1.114	420	2.764
120	1.376	540	3.249

Versuch 11. Substrat: [illegible]-Met[illegible]y-4-hydroxy-phenyläthyl-methyl-keton 2/10000 g. Mol. Laccase: 30 mg. Barometrischer [illegible]uck: 763.5 mm.

Tabelle 12.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.326 mg.	60 Min.	2.455 mg.
10	0.744	120	3.199
15	0.901	150	3.265
31	1.750	330	3.435

Versuch 12. Substrat: 3-Methoxy-4-hydroxy-phenyläthyl-octenyl-keton 2/10000 g. Mol. Laccase: 10 mg. Barometrischer Druck: 766.0 mm.

Tabelle 13.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	0.472 mg.	120 Min.	1.547 mg.
5	0.642	240	1.927
15	0.905	300	2.045
30	0.957	360	2.596
62	1.010	420	2.570

Versuch 13. Substrat: Pyrogallol 5/10000 g. Mol. Laccase: 10 mg. Barometrischer Druck: 761.2 mm. Nur bei diesem Versuch wurde neben dem Reaktionskolben noch ein kleiner Kolben mit KOH verwendet, um das sich entwickelnde CO_2-Gas[3] zu absorbieren.

Tabelle 14.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
8 Min.	0.260 mg.	302 Min.	8.970 mg.
15	1.263	360	9.452
30	2.005	472	10.715
60	4.062	555	11.665
120	6.067	ca. 23 Stdn. (nicht geschüttelt)	16.443
225	8.020		

(3) R. Willstätter und H. Heiss, *Ann.*, **433** (1923), 17.

Versuch 14. Substrat: *m*-Kresol 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 772.3 mm.

Tabelle 15.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
10 Min.	0.132 mg.	180 Min.	0.397 mg.
30	0.159	300	0.568
60	0.278	420	0.648
90	0.304	540	0.833
120	0.264		

Versuch 15. Substrat: Oxyhydrochinon-triacetat 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 761.6 mm.

Tabelle 16.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
3 Min.	2.709 mg.	180 Min.	10.199 mg.
9	4.403	240	10.499
15	5.575	300	10.773
30	7.581	360	10.799
60	8.949	420	11.137
90	9.522	480	11.228
120	9.861	525	11.359

Versuch 16. Substrat: Hydrochinon-monomethyläther 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 763.0 mm.

Tabelle 17.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
15 Min.	1.853 mg.	123 Min.	6.917 mg.
31	3.184	305	7.269
47	4.463	420	7.308
61	5.129	515	7.373

Versuch 17. Substrat: Diamidophenol-hydrochlorid 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 763.9 mm.

Tabelle 18.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
3 Min.	0.483 mg.	132 Min.	7.970 mg.
9	1.163	180	9.002
15	1.803	245	9.995
30	3.214	300	10.557
45	4.416	360	11.197
60	5 278	480	12.124
120	7.669	600	12.751

Versuch 18. Substrat: *p*-Phenylendiamin 5/10000 g. Mol. Laccase: 30 mg. Barometrischer Druck: 766.4 mm.

Tabelle 19.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
1 Min.	2.086 mg.	20 Min.	8.698 mg.
2	3.831	60	8.777
5	6.796	180	8.973
8	8.134	360	9.039
15	8.632	480	9.078

Versuch 19. Substrat: Dimethyl-*p*-phenylendiamin 5/10000 g. Mol. Laccase: 50 mg. Barometrischer Druck: 762.2 mm.

Tabelle 20.

Reaktionsdauer	O_2 absorbiert	Reaktionsdauer	O_2 absorbiert
2 Min.	5.006 mg.	123 Min.	11.146 mg.
5	7.717	180	11.602
7	8.108	210	12.410
10	8.473	300	13.349
30	9.151	420	14.366
60	9.660	540	14.809

Zum Schluss möchte ich den Herren T. Oshida und S. Yamane für ihre Hilfe, sowie der Keimeikai für ihre finanzielle Unterstützung bei Ausführung dieser Arbeit meinen herzlichen Dank ausdrücken.

Biochemisches Laboratorium der Kaiserlichen Landwirtschaftlichen Hochschule, Tottori.

THE EXCHANGE REACTIONS BETWEEN HEAVY WATER AND HYDROGEN COMPOUNDS.

By Eijiro OGAWA.

Received November 30th, 1935. Published March 28th, 1936.

I. Introduction. It was shown by many authors that hydrogen of polar radicals, such as $-NH_2$, $[NH_4]^+$, $-COOH$, undergoes an exchange with its isotope when dissolved in water containing heavy water. The author investigated these exchange reactions to study the differences of the exchangeabilities of these polar radicals quantitatively.

II. The Methods of the Experiment. Water containing 0.490 mol HDO (assuming that ordinary water contains 0.020 mol HDO), was prepared by electrolysis. Soluble hydrogen compounds were dissolved in this water (20–30 c.c.) and after the equilibrium attained, all the water was separated by distillation. Concentration of HDO was determined by measuring its specific gravity by the float method. The float, made of pyrex glass, has thin wall, which is crooked by a slight change of pressure. The measuring tube containing the float and water (about 15 c.c.) was immersed in Dewar vessel containing ice, and the pressure in the tube was regulated by the height of water column. Sensibility of the float is 1×10^{-6}. As water is separated by distillation, it is a fault of this experiment that the deviation of the equilibrium may take place due to the change in concentration during distillation.

III. The Order of the Exchange Reactions. In these experiments concentration of HDO is 0.490 mol. And it is assumed that only one of the hydrogen of polar radicals in one molecule will exchange when suitably great concentration of hydrogen compounds is used, although it is doubtful that in these isotopic exchange reactions the reaction proceeds strictly step by step.

For instance, in fructose the equilibrium constant of the reaction $5C_6H_{12}O_6 + 5HDO = 5C_6H_{11}DO_6 + 5H_2O$ is

$$K = \frac{[C_6H_{11}DO_6]^5 [H_2O]^5}{[C_6H_{12}O_6]^5 [HDO]^5}.$$

If it is assumed that the exchangeabilities of five OH-radicals are the same, then the equilibrium constant of the exchange reaction of each OH-radical must be expressed as follows:

$$K_{m_i} = \frac{[C_6H_{11}O_6D][H_2O]}{[C_6H_{12}O_6][HOD]} \quad (i = 1, 2, 3, 4, 5).$$

K_m is called the mean equilibrium constant. In this expression the concentration of $C_6H_{11}O_6D$ corresponds to 1/5 of the measured decrease of HDO concentration.[1] Then

$$K = K_{m_1}, \ K_{m_2}, \ K_{m_3}, \ K_{m_4}, \ K_{m_5}.$$

Generally, when, although each mean equilibrium constant is not the same, the differences are not so large, K_m approximately equals

$$\sqrt[n]{K_{m_1}K_{m_2}\cdots K_{m_n}} = \sqrt[n]{K}.$$

The results of the exchange reactions by 0.490 mol and 2.15 mols HDO are shown in Table 1.

Table 1.

Compound	Concentration (molarity)	Concentration of HDO (mol)	Decrease of conc. of HDO (mol)	Conc. of H_2O (mol)	K_m	Condition
Fructose	1.110	0.490	0.070	55.089	8.91	boiling 2 hrs.
,,	1.00	2.15	0.28	53.64	12.	,, 3 hrs.
NH_4Cl	8.149	0.490	0.115	55.134	2.10	,, 2 hrs.
,,	2.00	2.15	0.20	53.56	3.0	,, 3 hrs.

K_m are the equilibrium constants when the bimolecular reactions, such as $C_6H_{12}O_6 + HDO = C_6H_{11}DO_6 + H_2O$ and $NH_4Cl + HDO = NH_3DCl + H_2O$, are assumed. The separation of water is carried out by distillation, K_m must be somewhat larger than real values. Temperature range is 100°–120°C. Temperature regulation is not performed strictly as the temperature coefficients of the exchange are not large.

(1) The author made a mistake in the calculation of the equilibrium constant of the bimolecular exchange reaction in the previously published paper (*J. Chem. Soc. Japan*, **56** (1935), 1180.), and corrected in this paper as above by the kind advice of Mr. Masao Harada, Shiomi Institute, Osaka.

The value of K_m at 2.15 mols HDO is slightly larger indicating that the order of the reaction by 2.15 mols HDO tends to increase. However all the following results are deduced under the assumption that the exchange reaction at 0.490 mol HDO proceeds always bimolecularly.

IV. The Discussion of the So-called "Mean Equilibrium Constant." It may be pointed out in these experiments that the so-called equilibrium constants are somewhat larger owing to the deviation of the equilibrium according to change of concentration during distillation. The following experiments indicate to what extent this influence must be considered.

Urea. Urea is precipitated with $Hg(NO_3)_2$ as $CO(NH_2)_2 \cdot 2Hg(NO_3)_2$, which transforms into $CO(NH)_2 2HgNO_3$ liberating HNO_3. If a calculated quantity of $Hg(NO_3)_2$ is added to urea solution, all the urea is removed at once from the reaction system and the equilibrium constant in this case gives true one. The following results have been obtained at 22°, 80°, and 100°C.; at 22°C. the amount of HNO_3 liberated was very small, but with rising temperature its amount gradually increases. HNO_3 was neutralized with Na_2CO_3 and liberated H_2O was calculated as 0.020 mol HDO.

Table 2.

Temperature (°C.)	Concentration (molarity)	Concentration of HDO (mol)	Decrease in conc. of HDO (mol)	Conc. of H_2O (mol)	K_m	Condition
100	2.000	0.455	0.008	55.062	0.12	heating 3 hrs.
80	2.000	0.454	0.015	55.070	0.24	,, 3 hrs.
22	2.000	0.463	0.047	55.093	0.79	,, 1 day

K_m values decrease with rising temperature. Therefore it will be concluded that D content of HNO_3 liberated must be considerably large. K_m values obtained by distillation under reduced pressure at 50°C. and 100°C. are 0.71 and 0.50 respectively as indicated in Table 3. The value obtained by extrapolation to 22°C. from these values is 0.92 which is about 15% larger than the true equilibrium constant, namely, 0.79.

Ammonium Chloride. As the concentration of the solute in saturated solution is constant during distillation. The equilibrium constant obtained from saturated solution must be a nearly true constant when it is assumed that NH_4Cl in solid phase does not take part in the reaction. The constant at 100°C. becomes 0.47_7 which is about 10% larger than 0.52_6 for unsaturated solution. In general it is assumed that the so-called equilibrium constants are about 10–16% larger than the true ones.

Table 3.

Compound	Temp.	Conc. of compounds (molarity)	HDO conc. (mol)	Decrease in HDO conc. (mol)	H_2O conc. (mol)	K_m
$H_2NOH \cdot HCl$	100°	3.741	0.490	0.065	55.084	0.57
,,	100°	3.623	,,	0.065	55.084	0.59
$HClO_4$	100°	1.931	0.401	0.030	53.208	0.75
H_2SO_4	100°	8.590	0.479	0.118	46.635	0.45
H_3BO_3	100°	5.662	0.490	0.060	55.079	0.46
H_3PO_4	100°	9.199	0.415	0.061	55.155	0.34
NaOH	100°	17.498	0.490	0.064	55.083	0.21
NH_4Cl	100°	8.149	,,	0.115	55.134	0.52_6
,,	100°	14.449 (sat.)	,,	0.162	55.181	0.47_7
,,	70°	11.263 (sat.)	,,	0.133	55.152	0.46_1
$CO(NH_2)_2$	100°	8.326	,,	0.109	55.128	0.48
,,	100°	8.326	,,	0.117	55.136	0.52
,,	50°	8.326	,,	0.146	55.165	0.71
$C_6H_{12}O_6$ (fructose)	100°	1.110	,,	0.063	55.082	1.55
,,	50°	1.122	,,	0.051	55.070	1.19
COOH | COOH	100°	4.899	0.407	0.034	55.136	0.51
,,	50°	3.470	0.431	0.031	55.109	0.62
CH_2COOH | CH_2COOH	100°	6.353	0.490	0.043	55.062	0.42
CH_2 / CH_2–COOH CH_2 \ CH_2–COOH	100°	2.117	,,	0.015	55.034	0.41
CH_2–CH_2–COOH | CH_2–CH_2–COOH	100°	0.684	,,	0.007	55.026	0.5
COONa | COOH	100°	3.180	0.423	0.021	55.107	0.91
CH_2–COONa | CH_2–COOH	100°	2.952	0.471	0.011	55.049	0.4_5
CHCOOH ‖ HOOCCH	100°	0.689	0.490	0.008	55.028	0.6_5
CHCOOH ‖ CHCOOH	100°	2.154	,,	0.024	55.043	0.66
HOCHCOOH | CH_2COOH	100°	2.000	,,	0.021	55.040	0.41

Table 3. (*Concluded*)

Compound	Temp.	Conc. of compounds (molarity)	HDO conc. (mol)	Decrease in HDO conc. (mol)	H_2O conc. (mol)	K_m
HOCHCOOH | HOCHCOOH	100°	2.000	0.490	0.030	55.049	0.45
,,	50°	6.004	,,	0.095	55.114	0.56
CH_2–COOH | HOC–COOH | CH_2–COOH	100°	3.388	0.461	0.043	55.091	0.42
,,	50°	3.949	0.456	0.053	55.107	0.46
H_2NCH_2COOH	100°	2.256	0.490	0.034	55.053	0.62
,,	100°	3.331	,,	0.046	55.065	0.58
,,	50°	2.691	,,	0.057	55.076	0.92
,,	50°	3.331	,,	0.064	55.083	0.84
H_2O_2	50°	5.524	0.284	0.034	55.259	0.68
$C_6H_{12}O_6$ (glucose)	100°	1.110	0.498	0.031	55.042	0.67
,,	100°	1.110	0.396	0.028	55.141	0.77
,,	50°	1.092	0.396	0.045	55.158	1.35
CH_2OH | CHOH | CH_2OH	100°	4.978	0.362	0.049	55.196	0.59

V. The Relation between the Equilibrium Constants and Temperature. *Ammonium Chloride.* The equilibrium constant of the saturated solution is 0.47_7 at 100° and 0.46_1 at 70°C as indicated in Table 3. The relation between the equilibrium constant of the reaction $NH_4Cl+HDO = NH_3DCl+H_2O$ and temperature may be expressed by the following equation:

$$\log K_m = -\frac{300}{4.57T} - 0.146 .$$

The heat quantity 300 cal., that is the zero point energy difference between reacting components, indicates that this reaction is endothermic. The zero point energy difference between HDO and H_2O is 1700 cal., therefore the difference between NH_4Cl and NH_3DCl is 1400 cal.

Fructose. The so-called equilibrium constant is 1.55 at 100° and 1.19 at 50°C. From the expression

$$\log K_m = -\frac{1200}{4.57T} + 0.895$$

it follows that the reaction $C_6H_{12}O_6 + HDO = C_6H_{11}DO_6 + H_2O$ is endothermic.

The zero point energy difference between $C_6H_{12}O_6$ and $C_6H_{11}DO_6$ is 500 cal.

Oxalic Acid. The following expression was obtained from the so-called equilibrium constants at 100° and 50°C., the dissociation of oxalic acid being neglected:

$$\log K_m = \frac{900}{4.57T} - 0.815 .$$

The reaction $H_2C_2O_4 + HDO = HDC_2O_4 + H_2O$ is exothermic. The zero point energy difference between $H_2C_2O_4$ and HDC_2O_4 is 2600 cal.

Urea. The so-called equilibrium constant is 0.52 at 100° and 0.71 at 50°C. The zero point energy difference between $CO(NH_2)_2$ and $CO(NH_2)(NHD)$ was obtained as 3400 cal. from the following relations:

$$\log K_m = \frac{1700}{4.57T} - 1.296 .$$

VI. The Relation between the Mean Equilibrium Constants and Chemical Constitutions. Table 3 summarizes the results of exchange reactions between several hydrogen compounds and water containing 0.490 mol HDO. In these experiments almost all the water distilled over within 10 minutes under reduced pressure.

Now, for instance, in fructose, if each of five OH-radicals have the same chance of exchange independently, so the equilibrium constants 1.55 at 100°C and 1.19 at 50°C, can be regarded as the changeabilities.

However, as these calculations are based upon the assumption that the exchangeability is a function of each OH-group only, and independent of the structure of the molecule, these values are all approximate. In the case of glycocoll which has different polar radicals, $-NH_2$ and $-COOH$, in one molecule, it was assumed that the chances of exchange of $-NH_2$ and $-COOH$ are the same.

Hydroxylamine Hydrochloride. The mean value of the mean equilibrium constant at 100°C. is 0.58. If the constitution $H_3N{=}O^+HCl^-$ is assumed, there are two exchangeable radicals $H_3N{=}$ and ${=}OH^+$. If the exchangeability of $NH{\equiv}$ is assumed as 0.52 at 100°C. from the results of NH_4Cl, the exchangeability of $=OH^+$ becomes 0.80.

Strong Acids. Perchloric Acid. Assuming that perfect dissociation takes place and all the H becomes H_3O^+ in solution, the mean equilibrium constant 0.75 can be regarded as the exchangeability of $=OH^+$ which coincides with 0.80 for hydroxylamine hydrochloride. *Sulphuric Acid.* Assuming that the the primary dissociation is perfect and the secondary dissociation can be neglected, and taking the value 0.75 as the exchangeability of $=OH^+$, 0.1 was obtained as the exchangeability of HSO^-_4.

Weak Acids. Boric Acid. The mean equilibrium constant is 0.46, so the exchangeability of OH combined with B is 0.46 at 100°C. *Phosphoric Acid.* The mean equilibrium constant is 0.34, so the exchangeability of OH combined with P is 0.34 at 100°C.

Strong Base. Sodium Hydroxide. The value of K_m is 0.21. The exchangeability of OH^- is 0.21, assuming perfect dissociation.

Ammonium Chloride. The value of K_m is 0.52 in unsaturated solution. The exchangeability of $\equiv NH^+$ is 0.52 at 100° and 0.45 at 50°C.

Urea. The constitution of urea in neutral solution was assumed as $OC\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}$. The mean value of K_m is 0.50. The exchangeability of =NH combined with C is 0.50 at 100° and 0.71 at 50°C.

Fructose. The value of K_m is 1.55 at 100° and 1.19 at 50°C., so the exchangeability of –OH combined with C is 1.55 at 100° and 1.19 at 50°C.

Glucose. The value of K_m is 0.77 or 0.67 at 100° and 1.35 at 50°C. The values 1.55 and 1.19 for fructose are too large compared with other exchangeabilities. 0.72 is regarded as the exchangeability of –OH at 100°C. for this time.

Glycerine. The purity of glycerine used was 83.55%. K_m at 100°C. was 0.59.

Saturated Dicarboxylic Acids. Table 3 summarizes the results for oxalic acid, succinic acid, glutaric acid, and adipic acid. Malonic acid was excluded owing to its unstableness. The value of adipic acid is not so credible due to its low solubility.

If it is assumed that these values are in parallel with the strength of hydrogen bond in –COOH, it is concluded that the binding force of H in –COOH increases when the number of carbon atoms is increased from two to four, but does not change from four to five. The binding force is not influenced whether the number of carbon atoms in the chain is odd or even. If it is assumed that two carboxyl-groups in the molecule have the same

chance of exchange, the exchangeability of the carboxyl-group is obtained as 0.51 for oxalic acid and 0.42 for succinic acid. When Na is substituted for H of one of the carboxyl-groups in oxalic acid and succinic acid the exchangeability of H of the other –COOH becomes 0.91 for oxalic acid and 0.45 for succinic acid. The influence based upon the so-called "electron shift" due to highly ionisable character of Na-oxalate or Na-succinate can not be recognized obviously.

Unsaturated Dicarboxylic Acids. Fumaric Acid. The equilibrium constant was obtained as 0.6_5, although it can not be so credible a value because of the low solubility of the acid.

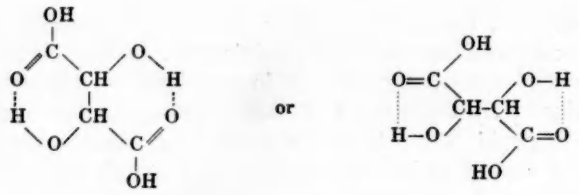
Maleic Acid. The mean equilibrium constant was obtained as 0.66 which is fairly high when compared with 0.42 for succinic acid. This behaviour is probably due to the existence of the double bond between two carbon atoms. The parallelism of the difference of properties between fumaric acid and maleic acid did not appear in this experiment.

Hydroxycarboxylic Acids. Malic Acid. The mean equilibrium constant is 0.41. If exchangeabilities of two carboxyl-groups are taken as 0.42 from succinic acid and the exchangeability of hydroxyl-group is taken as 1.55 from fructose, the calculated exchangeability of malic acid becomes $\sqrt[3]{0.42^2 \times 1.55} = 0.64$. When the exchangeability 0.72 for glucose is used, then $\sqrt[3]{0.42^2 \times 0.72} = 0.50$.

Tartaric Acid. The experimental value of the equilibrium constant at 100°C. is 0.45, the calculated value being $\sqrt[4]{0.42^2 \times 1.55^2} = 0.80$. The value of K_m at 50°C. is 0.56. The exchangeability of the carboxyl-groups at 50°C. may be estimated as 0.52 in connection with the exchangeability of oxalic acid and succinic acid at 100°C. The calculated value is $\sqrt[4]{0.52^2 \times 1.19^2} = 0.79$. When 0.72 is used for OH, then $\sqrt[4]{0.72^2 \times 0.42^2} = 0.55$ at 100°C.

Citric Acid. The experimental equilibrium constant is 0.42 at 100°C, the calculated value being $\sqrt[4]{1.55 \times 0.42^3} = 0.57$ or $\sqrt[4]{0.72 \times 0.42^3} = 0.48$. The equilibrium constant is 0.46 at 50°C, the calculated value being $\sqrt[4]{1.19^2 \times 0.52^2} = 0.64$. The specific rotation of *d*-tartaric acid decreases gradually with increasing concentration. Lowry and Austin[2] suggested that hydrogen atoms of hydroxyl-groups are co-ordinated with oxygen atoms of carboxyl-groups and assumed the existence of the following molecules in solution:

(2) Lowry and Auslin, *Nature*, **114** (1924), 431.



But the exchangeability of hydrogen in such a co-ordinated constitution must be lower than the hydrogen of free hydroxyl-radical. The results mentioned above do not favour this assumption.

Amino Acid. Glycocoll. The mean value of the experimental equilibrium constants is 0.59 at 100°C. and 0.88 at 50°C. The calculated value at 100°C. is $\sqrt[3]{0.50^2 \times 0.51} = 0.50$, if it is assumed that the exchangeabilities of –COOH and =NH are 0.51 from oxalic acid and 0.50 from urea, respectively. The calculated value of the exchangeability at 50°C. is $\sqrt[3]{0.71^2 \times 0.62} = 0.68$ in the same manner. These values do not coincide with the experimental ones. If glycocoll forms an intramolecular salt such as $\begin{matrix} H_2C\text{–}NH_3^+ \\ | \\ O{=}C\text{–}O^- \end{matrix}$, the calculated exchangeability of glycocoll becomes 0.52 at 100°C. from the value of NH_4Cl, while the calculated value 0.45 which is extrapolated from the values of NH_4Cl at 100°C. and 70°C. is by far smaller. Now if it is assumed that glycocoll can exist in two intramolecular salts:

$$\begin{matrix} H_2C\text{–}NH^- \\ | \\ O{=}C\text{–}OH_2^+ \end{matrix} \rightleftarrows \begin{matrix} H_2C\text{–}NH_3^+ \\ | \\ O{=}C\text{–}O^- \end{matrix}$$

and at 50°C. the left form is more probable, then calculated exchangeability becomes close to the experimental value. Namely, if the exchangeability of $=OH^+$ is taken as 0.80 at 100°C. as in hydroxylamine hydrochloride which may be slightly larger at 50°C., then the calculated value is $\sqrt[3]{0.71 \times 0.80^2} = 0.77$.

Hydrogen Peroxide. The mean equilibrium constant is 0.68 at 50°C. The exchangeability of –OH of water is assumed 1.00. If the constitution of H_2O_2 is assumed as H–O–O–H, the value of K_m is 1.00, and if the constitution $\begin{matrix} O\text{–}H \\ \| \\ O\text{–}H \end{matrix}$ or $\begin{matrix} O \\ \| \\ H\text{–}O\text{–}H \end{matrix}$ is assumed, the exchangeability of $\equiv OH$ is the same as $=OH^+$ from hydroxylamine hydrochloride, and then the exchangeability

becomes 0.80. When the co-ordinated formula such as $\begin{matrix} & O & \\ \diagup & & \diagdown \\ H & - & O - H \end{matrix}$ is assumed, the exchangeability of co-ordinated hydrogen must be smaller, therefore in this connection the above formula is very probable for H_2O_2.

VII. The Comparison of the Exchangeabilities. Table 4 summarizes the exchangeabilities of the different radicals. The exchangeability of each

Table 4.

Radical	Temperature	
	100°C.	50°C
−OH (alcoholic)	1.55 or 0.72	1.19
−OH (water)	1.00	
$=OH^+$ (hydroxylamine hydrochloride)	0.80	
−OH (boric acid)	0.46	
−OH (phosphoric acid)	0.34	
$\equiv NH^+$ (ammonium chloride)	0.52	0.45
=NH (urea)	0.50	0.71
−COOH (oxalic acid)	0.51	0.62
−COOH (succinic acid)	0.42	
−COOH (maleic acid)	0.66	
−COOH (Na oxalate)	0.91	
−COOH (Na-succinate)	0.4_5	
HSO_4^- (sulphuric acid)	0.1	
OH^- (sodium hydroxide)	0.2	

radical depends upon the differences of zero point energies between H-substituted radical and D-substituted radical, for instance, –OH and –OD. The greater the difference of zero point energies, the smaller the above-mentioned exchangeability. The exchangeability is a measure of the strength of the chemical bindings. The exchangeability depends upon not only the element with which hydrogen is combined, but also the kind and the valency state of the element to which the radical is connected. Namely among the exchangeabilities of $-OH^-$, =NH and –COOH, combined with the carbon atom, that of –OH is the largest and that of –COOH the smallest.

When the element with which the radicals are combined differ, the exchangeabilities are as follows: H–OH 1.00, C–OH 0.72, B–OH 0.46, P–OH 0.34. And further the experiments upon the exchangeability of saturated dicarboxylic acids and unsaturated dicarboxylic acids show that the influence of the length of the chain upon the exchangeabilities of

–COOH disappears when the number of carbon atom is increased to four and the double bond increases the exchangeability slightly.

The influence of "electron shift" due to dissociation is obviously recognized in the cases of HSO_4^- and OH^-. In this connection the polarities of the radicals must have some influences upon their exchangeabilities. The parallelism between exchangeability and polarity or Raman frequency cannot be discussed perfectly owing to the lack of suitable data.

VIII. Applications. In the exchange reactions between soluble hydrogen compounds and water containing 0.490 mol HDO, the second order reaction being assumed, the exchangeabilities of polar radicals have been found quantitatively. These exchangeabilities are the measure of the differences of the zero point energies or chemical binding forces. By using these values, the exchangeability of any substance of the known constitution may be found and moreover the determination of the kind or the number of polar radicals of an unknown substance may be possible. The interchange of isotopes does not affect the valency state at all, so it is a most trustworthy way to apply these data to the determination of the constitution, as shown in the cases of hydroxycarboxylic acids, glycocoll, and H_2O_2. Further, these data also suggest the possible method of the isolation of other isotopes.

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